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Oxidative Coupling Reactions of 1,3-Diarylpropene Derivatives to Dibenzo[*a*,*c*]cycloheptenes by PIFA

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The oxidative cyclization reactions of a variety of α-benzylcinnamates can be selectively performed with hypervalent iodine as an oxidant. The dibenzo[*a*,*c*]cycloheptenes were isolated in up to 55 % yield. When an oxo substrate is applied, the yield was significantly increased. With this synthetic approach, a central intermediate for the synthesis of metasequirin-B was obtained in three steps from very simple starting materials. For this transformation, both aryl moieties have to be activated.

Introduction

Several natural products exhibiting seven-membered ring systems with annulated benzo moieties are known among the cycloneolignans and alkaloids,[1] the most prominent example of which is colchicine.[2] This natural product and its related compounds, such as allocolchicine, have experienced significant medicinal and biological interest because of their pharmacological potential.[3] According to their known mode of action, colchicine and its analogues bind to the β-subunit of the protein tubulin in the protofilaments, which results in the destabilization of the microtubules.[4] This efficiently inhibits the formation of the mitotic spindle in eukaryotic cells and is of potential interest for applications in cancer therapy. The high toxicity of colchicine limits its application and creates a demand for structural analogues. Metasequirin-B is the only known naturally occurring norcycloneolignan with a dibenzocycloheptene skeleton fused with a tetrahydrofuran (THF) system. This natural product is found in the heartwood of *Metasequoia glyptostroboides*.[5] The similar architecture of metasequirin-B to allocolchicine suggests an interesting pharmacological profile (Figure 1). These compounds are considered as vascular disrupting agents because of the tubulin-binding mechanism, whereas antiangiogenesis drugs act as vascular disrupting agents on existing blood vessels, which feed a solid tumor causing a tumor ischemia and necrosis. In particular, these potential drugs are of interest for the nonsurgical treatment of advanced cancer states.[6] Consequently, access to the dibenzo[*a*,*c*]cycloheptene skeleton is highly desired.

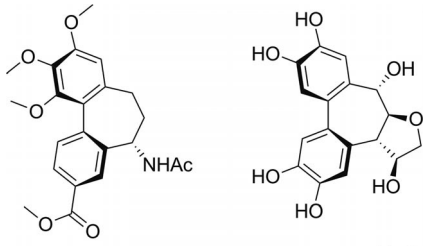

Figure 1. Structure of allocolchicine and metasequirin-B.

Common synthetic strategies exploit an early construction of the biaryl moiety. Subsequently, the central seven-membered ring is accomplished. This approach to tricyclic compounds usually requires several steps and is less flexible for molecular variations.[7] An oxidative cyclization approach via diaryl substrates seems to be ideal because of its atom-economic nature. It is noteworthy that this technology has received less attention due to the low yields that are usually observed for such reactions.[8] The only example of an unsaturated diaryl substrate has been achieved by the toxic reagent thallium(III) trifluoroacetate (TTFA) and was not extended to a general method.[9] When 1,3-diarylpropanes are available, $MoCl_5$ is a powerful oxidant providing a collection of dihydrodibenzo[*a*,*c*]cycloheptenes with different substitution patterns.[10]

For the oxidative coupling reaction, $MoCl_5$ is a versatile and easy to handle reagent.[11–13] The performance of this reagent can be enhanced when Lewis acids are used to bind

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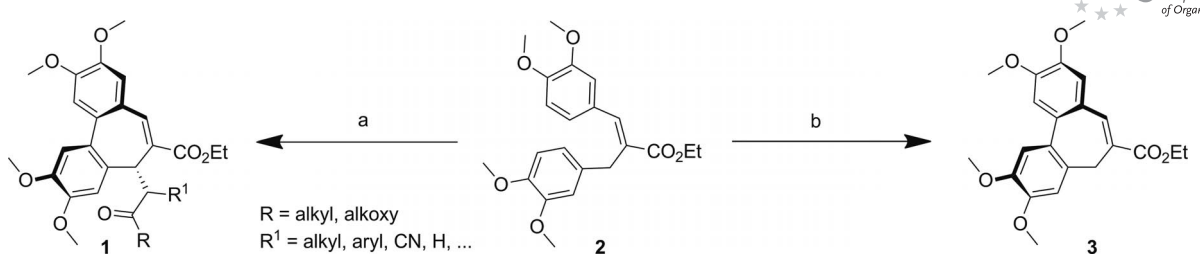
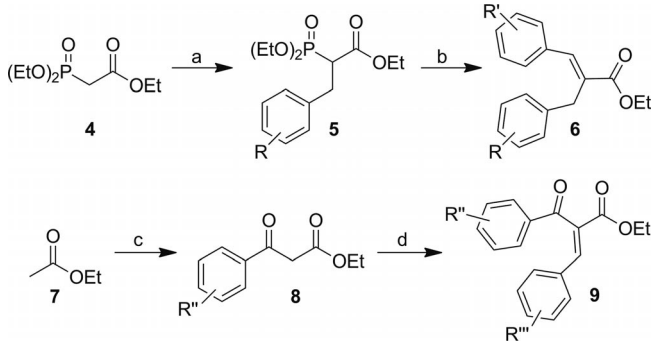


Scheme 1. Oxidant-dependant reaction pathway: (a) $MoCl_5$, $TiCl_4$ then R^1CH_2COR, NEt_3; (b) PIFA, $BF_3{\cdot}OEt_2$.

hydrogen chloride.[14] If α-benzylcinnamic acid derivatives **2** are subjected to this reagent mixture, overoxidation occurs, and an oxidative domino coupling follows resulting in the formation of **1** (Scheme 1). An intermediate tropylium species is postulated, which allows the installation of a carbon side chain.[15]

Here we report an oxidative coupling protocol, which stops at the intramolecular arylation product **3**. The method of choice is based on Kita's hypervalent iodine reagent phenyliodine(III) bis(trifluoroacetate) (PIFA).[16] Other reagents, such as $FeCl_3$ or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, resulted either in no conversion, complete decomposition, or in the case of $MoCl_5$, proceeded with further C–H functionalization.[15] The unusually high oxidation power was also found by King et al.[12,13] Substrates **2** and **6** are readily prepared by a benzylation/olefination sequence starting with phosphonoacetate **4** (Scheme 2). The introduction of the benzyl moiety was best performed in *N*,*N*-dimethylformamide (DMF) in the presence of K_2CO_3 and the corresponding benzyl chloride derivative. Yields for the α-phosphono-dihydrocinnamates **5** are up to 68%. The synthesis of the product can be easily conducted on a 0.1 M scale (Supporting Information). Suitable conditions for the Horner–Wadsworth–Emmons olefination employ sodium hydride in toluene. However, our previously elaborated protocol for the synthesis of α-arylcinnamates could not be employed in the synthesis of **6**.[17]



Scheme 2. Synthesis of the substrates: (a) K_2CO_3, benzyl chloride derivative, DMF, room temp.; (b) NaH, benzaldehyde derivative, toluene, 50 °C; (c) LDA, benzoyl chloride derivative; THF, –70 °C; (d) pyridine, AcOH, benzaldehyde derivative, benzene, reflux.

For the oxo substrates **9** a two-step sequence including benzoylation and Knoevenagel condensation was applied.[18] Standard conditions resulted in yields of up to 84% for the substituted ethyl benzoylacetates **8** and up to 89% for the ethyl α-benzoylcinnamates **9**.[19]

Results and Discussion

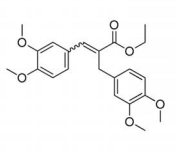
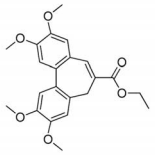
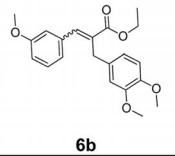
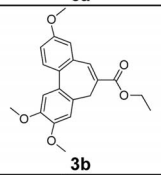
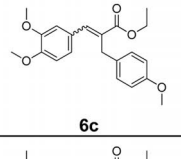
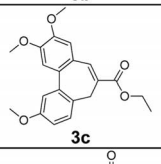
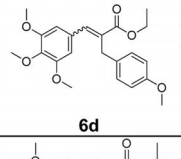
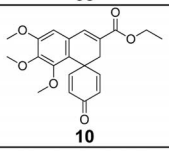
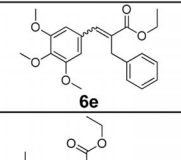
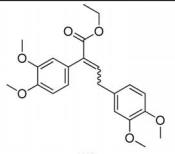
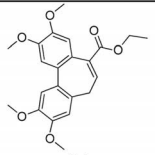
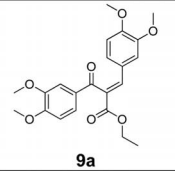
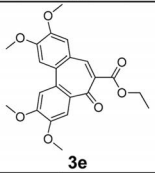
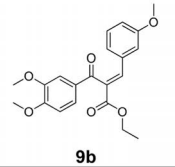
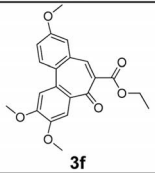
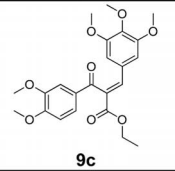
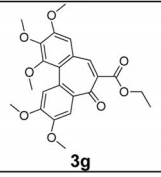
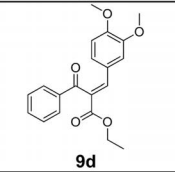
The tetramethoxy substrate **6a** exhibits optimal activation in both aryl moieties for the oxidation coupling process. The product **3a** with the seven-membered ring system was isolated in 55% yield (Table 1, Entry 1). The reaction was conducted at low temperature for 1.5 h and then at room temperature for 0.5 h prior to workup. The molecular structure was verified by X-ray analysis of a suitable single crystal. The central seven-membered ring is strongly bent and shows a boat-type conformation (Figure 2), and the biaryl axis is tilted by about 38°.

The location of the electron-releasing methoxy groups is important. In **6b** only a single methoxy group is present on the cinnamate, whereas the intramolecular coupling partner exhibits both methoxy groups. Compared to **6a**, the reactivity of **6b** is significantly decreased. The desired dibenzo[*a*,*c*]-cycloheptene **3b** was obtained in 31% yield (Entry 2). A reversed substitution pattern with two methoxy groups on the cinnamate and one on the benzyl moiety was beneficial for the oxidative arylation. The electron-withdrawing nature of the ester functionality is partially compensated and resulted in 51% yield for **6c**, and 29% of the starting material was recovered (Entry 3).

The limits of this transformation were elucidated by variation of the molecular structure. Further methoxy groups on the cinnamate portion led to another reaction pathway. Spirocyclohexadienone derivative **10** was isolated in 59%. The loss of the methyl group occurs on the benzyl moiety (Entry 4). The architecture of **10** was elucidated by X-ray analysis of a suitable single crystal (Figure 3).

Most probably, the steric strain caused by the formation of the seven-membered ring system adjacent to the methoxy substitutions is too high. Consequently, the six-membered ring is preferred. If the benzyl fragment is not equipped with an electron-releasing group, no cyclization reaction was detected (Entry 5). Shifting the ester group adjacent to the benzo ring in **6f** is rewarded by a lower yield and a mixture of atropisomers, as these groups exhibit limited ro-

Table 1. Oxidative cyclization by PIFA/BF_3·OEt_2 (optimized conditions).

Entry	Substrate	Product	Method[a]	Time[b]	Yield
1	 **6a**	 **3a**	B	1.5 h 30 min	55%
2	 **6b**	 **3b**	B	1.5 h 30 min	31%
3	 **6c**	 **3c**	A	40 min 1 h	51% (29% **6c**)
4	 **6d**	 **10**	A	40 min	59%
5	 **6e**	–	A	1 h	–
6	 **6f**	 **3d**	B	2 h 1.5 h	21%[c]
7	 **9a**	 **3e**	A	40 min	84% 73%[d]
8	 **9b**	 **3f**	A	1h 1h	51%
9	 **9c**	 **3g**	B	45 min 45 min	10%
10	 **9d**	–	A	40 min	–

[a] Method A: –40 °C to room temp.; Method B: –20 °C to room temp. [b] First, reaction time at low temperature, then additional reaction time at room temp. given. [c] Ratio of isomers 2:1. [d] After crystallization from ethyl acetate.

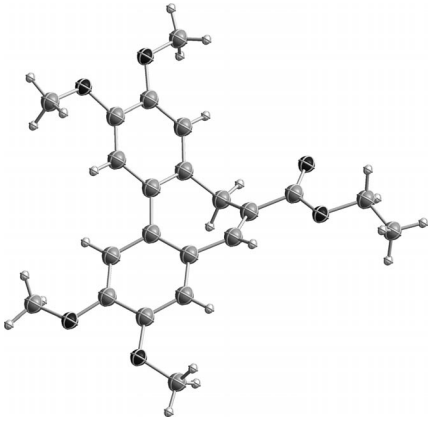


Figure 2. Molecular structure of **3a** obtained by X-ray analysis.

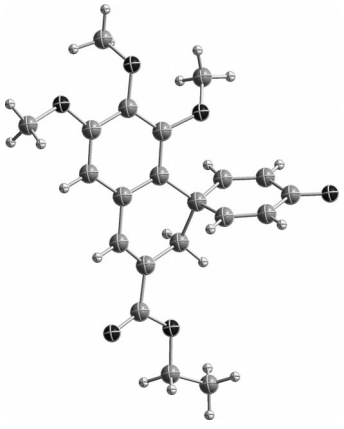


Figure 3. Molecular structure of **10** obtained by X-ray analysis.

tational freedom at the seven-membered ring (Entry 6). Installation of an additional oxo group on the substrate is beneficial to the oxidative coupling process. Despite its electron-withdrawing nature, yields are increased compared to the methylene-equipped congeners. The products have some aromatic stabilization from the central tropylium system. Substrate **9a** is oxidatively arylated to **3e** in 84% yield. Upon crystallization from ethyl acetate, some loss of product occurs (Entry 7). When **9b** is treated in an analogous way, the dibenzo[*a*,*c*]cycloheptenone **3f** is obtained in 51% yield (Entry 8). As **6b** represents the nonoxygenated equivalent of **9b**, the influence of the oxo function is remarkable. The molecular structure of **3f** was elucidated by X-ray analysis of a suitable single crystal. Two competing effects have an influence on the structure: first, stabilization is achieved by formation of a central tropylium-like system leading to a more planarized core; secondly, the steric strain caused by the set of substituents arranged around the seven-membered ring system will disfavor the generation of the central tropylium-like system. The molecular structure of **3f** exhibits a strongly planarized central ring system (Figure 4), and the birayl axis is tilted by about 28°.

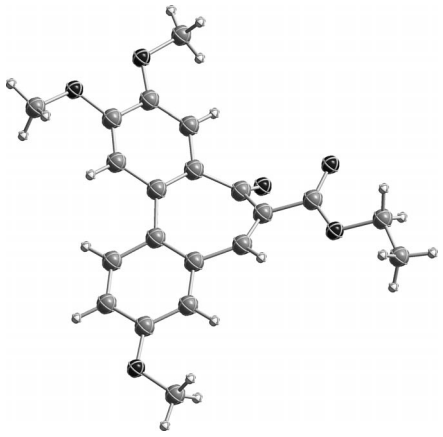


Figure 4. Molecular structure of **3f** obtained by X-ray analysis.

A substrate with a trimethoxyphenyl moiety (**9c**) still gives access to the seven-membered ring system. Although the yield is low, the attack adjacent to the carbonyl group is efficiently inhibited (Entry 9). Extension of this method to a substrate with a coupling partner without an activating group results in no conversion as deactivation by the attached carbonyl group is too high (Entry 10).

Conclusions

The cyclization reaction to dibenzo[*a*,*c*]cycloheptenes and dibenzo[*a*,*c*]cycloheptenones by oxidative biaryl coupling is best achieved by the use of hypervalent iodine reagents. The Kita-type protocol allows the formation of the central seven-membered ring in good to acceptable yields. The benzo rings fused at *a* and *c* disfavor a planar geometry. However, the use of substrates with an oxo functionality results in significantly better yields. The starting materials are readily prepared and can be constructed in a modular fashion. However, for both classes of substrates both aryl moieties have to be activated by at least one methoxy group in order to be suitable for oxidative cyclization. The central intermediate for the synthesis of metasequirin-B was obtained in three steps from very simple starting materials with this synthetic approach.

Experimental Section

General Remarks: See Supporting Information.

Ethyl 2-(Diethoxyphosphoryl)-3-(4-methoxyphenyl)propanoate (5b): Ethyl (diethoxyphosphoryl)acetate (**4**, 5 g, 22.3 mmol), 1-(chloromethyl)-4-methoxybenzene (1.75 g, 11.15 mmol), and K_2CO_3 (2.31 g, 16.73 mmol) in anhydrous DMF (50 mL) were stirred at room temperature for 3 d. Water (300 mL) was added, and the aqueous layer was extracted with ethyl acetate (5× 30 mL). The combined organic fractions were washed with water (50 mL) and brine (50 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Excess **4** was removed by distillation under high vacuum (56 °C, 0.4 mbar, 120 °C). The crude benzylation product was purified by distillation (62 °C, 2.5×10^{-6} mbar, 170 °C), which yielded 2.06 g (54%) of the desired product. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (t, $^3J_{4,3}$ = 7.1 Hz, 3 H), 1.34 (t, $^3J_{6,5}$ = 7.1 Hz, 3 H), 1.35 (t, $^3J_{8,7}$ = 7.1 Hz, 3 H), 3.07–3.27 (m, 3× 1 H), 3.77 (s, 3 H), 4.05–4.22 (m, 3× 2 H), 6.80 (d, $^3J_{12,11}$ = 9.0 Hz, 2× 1 H), 7.10 (d, $^3J_{11,12}$ = 9.0 Hz, 2× 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (s), 16.3 (d, $^3J_{8,P}$ = 6.1 Hz), 16.4 (d, $^3J_{6,P}$ = 6.1 Hz), 32.0 (d, $^2J_{9,P}$ = 4.4 Hz), 48.0 (d, $^1J_{1,P}$ = 128.5 Hz), 55.2 (s, C-14), 61.3 (s), 62.7 (d, $^2J_{7,P}$ = 6.9 Hz), 62.8 (d, $^2J_{5,P}$ = 6.5 Hz), 113.9 (s), 129.6 (s), 130.6 (d, $^3J_{10,P}$ = 16.6 Hz), 158.3 (s), 168.5 (d, $^2J_{2,P}$ = 4.6 Hz) ppm. MS (EI, 70 eV): *m*/*z* (%) = 344 (38) $[M]^{+\cdot}$, 299 (10) $[M - C_2H_5O]^+$, 271 (63) $[M - C_2H_5O - CO]^+$, 243 (8) $[M - C_2H_5O - CO - C_2H_4]^+$, 206 (100) $[M - OP(OC_2H_5)_2 - H]^{+\cdot}$, 161 (82) $[M - OP(OC_2H_5)_2 - H - OC_2H_5]^+$, 134 (35) $[C_9H_{10}O]^+$, 121 (58) $[C_8H_9O]^+$, 91 (7) $[C_6H_3O]^+$, 77 (69) $[C_6H_5]^+$. HRMS (EI): calcd. for $C_{17}H_{27}O_7P$ $[M]^{+\cdot}$ 344.1389; found 344.1387.

Ethyl (2*E*)-3-(3,4-dimethoxyphenyl)-2-(4-methoxybenzyl)prop-2-enoate (6c): To **5c** (450 mg, 1.30 mmol) and 3,4-dimethoxybenzaldehyde (249 mg, 1.50 mmol) in anhydrous toluene (10 mL) was added NaH (57 mg, 60% in mineral oil, 1.43 mmol) in several portions with stirring at room temperature. The mixture was then stirred at room temperature for 4 d. The solvent was removed under reduced pressure, and the residue was taken up in ethyl acetate (20 mL) and washed with water (10 mL). The separated aqueous fraction was extracted with ethyl acetate (3× 15 mL). The combined organic fractions were washed with brine (25 mL) and dried with $MgSO_4$. Removal of the solvent under reduced pressure and purification by column chromatography on silica (cyclohexane/ethyl acetate, 4:1) yielded a 4:1 mixture of (*E*)/(*Z*) isomers (430 mg, 90%) as a yellow solid. The major product is (*E*) isomer. **(*E*)-6c:** R_F (SiO_2; cyclohexane/ethyl acetate, 4:1) = 0.33. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, $^3J_{5,4}$ = 7.1 Hz, 3 H), 3.66 (s, 3 H), 3.78 (s, 3 H), 3.88 (s, 3 H), 3.95 (br. s, 2× 1 H), 4.23 (q, $^3J_{4,5}$ = 7.1 Hz, 2 H), 6.83 (d, $^3J_{9,8} \approx {}^3J_{5',6'}$ = 8.8 Hz, 3× 1 H), 6.90 (d, $^4J_{2',6'}$ = 2.7 Hz, 1 H), 7.00 (dd, $^3J_{6',5'}$ = 9.0 Hz, $^4J_{6',2'}$ = 2.7 Hz, 1 H), 7.13 (d, $^3J_{8,9}$ = 8.8 Hz, 1 H), 7.87 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 32.3, 55.1, 55.5, 55.8, 60.7, 110.9, 112.3, 113.9, 122.9, 128.7, 128.9, 131.4, 140.4, 148.6, 149.5, 157.9, 168.4 ppm. **(*Z*)-6c:** ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (t, $^3J_{5,4}$ = 7.1 Hz, 3 H), 3.66 (br. s, 2× 1 H), 3.77 (s, 3 H), 3.84 (s, 3 H), 3.86 (s, 3 H), 4.07 (q, $^3J_{4,5}$ = 7.1 Hz, 2 H), 6.51 (br. s, 1 H), 6.76–6.90 (m, 5× 1 H), 7.17 (d, $^3J_{8,9}$ = 8.4 Hz, 2× 1 H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.8, 40.6, 55.2, 55.7, 55.8, 60.5, 110.6, 111.4, 113.8, 121.4, 130.0, 130.0, 131.1, 132.9, 133.6, 148.3, 148.8, 158.2, 169.5 ppm. MS (EI, 70 eV): *m*/*z* (%) = 356 (100) $[M]^{+\cdot}$, 327 (5) $[M - C_2H_5]^+$, 311 (10) $[M - C_2H_5O]^+$, 282 (70) $[M - C_2H_5O - CO - H]^{+\cdot}$, 267 (30) $[M - C_2H_5O - CO - H - CH_3]^+$, 251 (11) $[M - C_2H_5O - CO - H - OCH_3]^+$, 236 (13) $[M - C_2H_5O - CO - H - OCH_3 - CH_3]^{+\cdot}$, 210 (13), 189 (17) $[M - C_2H_5O - CO - H - OCH_3 - OCH_3 - OCH_3]^+$, 165 (18) $[C_{13}H_{10}]^+$, 145 (10) $[C_{10}H_9O]^+$, 121 (11) $[C_8H_9O]^+$, 77 (66) $[C_6H_5]^+$. HRMS (EI): calcd. for $C_{21}H_{24}O_5$ $[M]^{+\cdot}$ 356.1624; found 356.1620. $C_{21}H_{24}O_5$ (356.42): calcd. C 70.77, H 6.79; found C 70.96, H 6.98.

Ethyl (2*E*)-2-(3,4-Dimethoxybenzoyl)-3-(3,4-dimethoxyphenyl)prop-2-enoate (9a): The Knoevenagel condensation was carried out with ethyl 3-(3,4-dimethoxyphenyl)-3-oxopropanoate (**8**, 600 mg, 2.38 mmol), 3,4-dimethoxybenzaldehyde (395 mg, 2.38 mmol), AcOH (0.03 mL, 0.48 mmol), and piperidine (0.02 mL, 0.24 mL) in benzene (20 mL) with a Dean–Stark apparatus. After 4 h of heating to reflux, the mixture was allowed to cool to ambient temperature before water (20 mL) was added. The separated aqueous fraction was extracted with *tert*-butyl methyl ether (TBME) (3× 20 mL), and the combined organic fractions were washed with 1 N HCl (2× 20 mL), satd. $NaHCO_3$ (20 mL), and brine (20 mL), and dried with

$MgSO_4$. Removal of the solvent under reduced pressure and purification by column chromatography on silica (cyclohexane/ethyl acetate, 2:1) yielded a single diastereomer (840 mg, 88%) as a yellow solid. R_F (SiO_2; cyclohexane/ethyl acetate, 2:1) = 0.17. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.20 (t, $^3J_{5,4}$ = 7.1 Hz, 3 H), 3.61 (s, 3 H), 3.82 (s, 3 H), 3.90 (s, 3 H), 3.91 (s, 3 H), 4.22 (q, $^3J_{4,5}$ = 7.1 Hz, 2 H), 6.74 (d, $^3J_{5',6'}$ = 8.4 Hz, 1 H), 6.80 (d, $^3J_{11,12}$ = 8.4 Hz, 1 H), 6.84 (d, $^4J_{2',6'}$ = 2.1 Hz, 1 H), 6.99 (dd, $^3J_{6',5'}$ = 8.5, $^4J_{6',2'}$ = 2.0 Hz, 1 H), 7.50 (dd, $^3J_{12,11}$ = 8.4, $^4J_{12,8}$ = 2.0 Hz, 1 H), 7.61 (d, $^4J_{8,12}$ = 2.0 Hz, 1 H), 7.85 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 55.5, 55.8, 56.0, 56.0, 61.3, 110.0, 110.2, 110.8, 112.3, 124.9, 124.9, 125.8, 128.8, 129.6, 142.0, 148.7, 149.3, 150.9, 154.0, 165.4, 194.6 ppm. MS (EI, 70 eV): *m*/*z* (%) = 400 (83) $[M]^{\cdot+}$, 354 (60) $[M - C_2H_5O - H]^{\cdot+}$, 326 (75) $[M - C_2H_5O - H - CO]^{\cdot+}$, 299 (30) $[M - C_2H_5O - CO - CO]^+$, 165 (100) $[C_9H_9O_3]^+$. HRMS (EI): calcd. for $C_{22}H_{24}O_7$ $[M]^{\cdot+}$ 400.1522; found 400.1521. $C_{22}H_{24}O_7$ (400.43): calcd. C 65.99, H 6.04; found C 65.27, H 6.08.

Ethyl 2,3,9,10-Tetramethoxy-5*H*-dibenzo[*a*,*c*][7]annulene-6-carboxylate (3a): The oxidative coupling was carried out under an inert gas with a solution of **9a** (158 mg, 0.41 mmol) in anhydrous dichloromethane (6 mL) at –20 °C. A solution of PIFA (194 mg, 0.45 mmol) and $BF_3{\cdot}OEt_2$ (0.21 mL, 0.82 mmol) in anhydrous dichloromethane (6 mL) was prepared separately and added by syringe to the chilled substrate over a period of 20 min. After the mixture had been stirred for 1.5 h, it was warmed to ambient temperature, and stirring was continued for another 30 min. The reaction was quenched by the addition of satd. $NaHCO_3$ solution (10 mL). The separated aqueous fraction was extracted with ethyl acetate (3 × 10 mL). The combined organic fractions were washed with brine (10 mL) and dried with anhydrous $MgSO_4$. The crude product was purified by flash column chromatography on silica (cyclohexane/ethyl acetate, 3:1), which yielded 86 mg (55%) of the desired product as a slightly yellow solid. Single crystals of **3a** were obtained by diffusion of *n*-heptane to a solution of **3a** in dichloromethane at ambient conditions. R_F (SiO_2; cyclohexane/ethyl acetate, 3:1) = 0.22. M.p. 146 °C (CH_2Cl_2/*n*-heptane). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.34 (t, $^3J_{13,12}$ = 7.1 Hz, 3 H), 2.74 (br. s, 1 H), 3.81–3.86 (m, 1 H), 3.89 (s, 3 H), 3.91 (s, 3 H), 3.94 (s, 3 H), 3.99 (s, 3 H), 4.26 (q, $^3J_{12,13}$ = 7.1 Hz, 2 H), 6.85 (s, 1 H), 6.91 (s, 1 H), 6.99 (s, 1 H), 7.15 (s, 1 H), 7.58 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3, 31.4, 55.9, 55.9, 56.0, 56.2, 60.7, 110.4, 111.7, 112.3, 112.6, 127.3, 129.8, 131.0, 133.2, 134.2, 136.5, 147.5, 147.6, 148.9, 149.2, 166.1 ppm. MS (EI, 70 eV, 120 °C): *m*/*z* (%) = 384 (70) $[M]^{\cdot+}$, 355 (30) $[M - C_2H_5]^+$, 339 (10) $[M - C_2H_5O]^+$, 311 (100) $[M - C_2H_5 - CO_2]^+$, 267 (17) $[C_{16}H_{11}O_4]^+$, 225 (7), 181 (8), 152 (9). HRMS (EI): calcd. for $C_{22}H_{24}O_6$ $[M]^{\cdot+}$ 384.1573; found 384.1574. $C_{22}H_{24}O_6$ (384.43): calcd. C 68.10, H 5.99; found C 68.32, H 6.19.

CCDC-827036 (for **3a**), -827037 (for **3f**), and -827038 (for **10**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): Additional experimental procedures, complete assignment of NMR spectroscopic data, analytical data for all products and intermediates.

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