EurJOC
European Journal of Organic Chemistry

Research Article
doi.org/10.1002/ejoc.202301052

Chemistry Europe
European Chemical Societies Publishing

www.eurjoc.org

Synthesis of the Altertoxin I Framework

Maximilian Gutsche,[a] Dominik Pfaff,[a] and Joachim Podlech*[a]

Routes to the framework of perylenequinone-derived mycotoxins of the biphenyl type are described. 1,2,11,12-Tetrahydroperylenequinone is most suitably prepared in seven steps starting with 3-hydroxyacetophenone. Key steps are an Ullmann coupling, pinacol-type cyclization, bromination, enolate reaction, and intramolecular Friedel-Crafts cyclization. A second approach starting with 1,5-dihydroxynaphthalene yields the respective decarbonylated core. Key steps of this 5-step sequence are again an Ullmann coupling and a McMurry olefination. The cleavage of the preferentially utilized hexyl protecting group could be achieved with boron bromide.

Introduction

A number of natural products are derived from perylenequinone and thus from the parent perylene. Two major classes of natural products can here be differentiated, where representatives of the first one generally show intact, fully conjugated perylenequinone moieties. Typical natural products of this type are the calphostins[1] or the hypocrellins (Figure 1),[2] where quite a number of total syntheses have been presented for this class of natural products.[3] Members of a second class of perylenequinone-derived natural products do not show full conjugation in the carbon core; they are partially reduced to di-, tetra-, or hexahydroperylenequinones. Furthermore, they do not bear additional carbon substituents and thus the twenty carbon atoms of the parent perylene are only augmented by the occasional presence of *O*-alkyl groups, especially of methylated hydroxy groups. These compounds have in common that they seem generally to be fungal metabolites and their toxicity is thus of relevance in invested food and feed. No total synthesis has been published for any of these compounds, although we are aware of some efforts made in the group of the late Karsten Krohn.[4] These mycotoxins can furthermore be categorized in a number of sub-classes,[5] where the most relevant toxins either belong to the 1) biphenyl type, in which two fully intact benzene rings are present in a stacked orientation (e.g., altertoxin I, II, or stempyltoxin I), or 2) to the dihydroanthracene type, where two diagonally arranged benzene rings are present (e.g. altertoxin III). An overview on perylene-derived mycotoxins has been published only recently.[6]

In this manuscript we describe approaches to the altertoxin I framework, i.e., to the core of the biphenyl-derived toxins. Our synthetic efforts towards the altertoxin III core are summarized in a further publication.[7]

Results and Discussion

In this manuscript we describe four routes leading to frameworks **A** and **F** common to the perylene-derived mycotoxins of the biphenyl type. The retrosynthesis for these routes is given in Scheme 1. A first approach consists of a double intramolecular Friedel-Crafts-type acylation using suitable carboxylic esters **B** or similarly activated intermediates. These diesters **B** should be either accessible by reaction of an appropriate biphenyl **C** with an alkyne **D** (route A) or by modification in 9,10 positions of a suitable phenanthrene precursor **E** (route B). The key step of a further approach (route C) would be a McMurry reaction of diketone **G** furnishing pentacycle **F**. Intermediate **G** could be obtained by reductive coupling of a halogenated precursor **H**. A last approach (route D) discussed herein includes Grignard additions to a perylenequinone **I**, which might be accessible by intramolecular Stetter reaction of **J**. Dialdehyde **J** could be obtained by Ullman coupling of precursor **K**.

Following route A we needed a suitably substituted biphenyl precursor **C**. Methoxy groups in the *para* positions of the biphenyl should be cleaved in a late stage of the total synthesis which would liberate the hydroxy groups at the respective positions in the perylenequinone derivatives. Further substituents in one or two of the biphenyl's *ortho* positions should allow for [4+2] cyclizations with alkynes. A plethora of methods had been proposed for the transformation of biphenyl derivatives with alkynes to yield phenanthrene derivatives. We picked three of these methods: a first one, in which an *ortho*-iodinated biphenyl **8** is used as precursor, a second approach using a 2,2′-diiodinated biphenyl derivative **9**, and a last method utilizing carboxylic acid **24**.

We started with commercially available 4-methoxy-2-nitroaniline (**1**), which was subjected to a Sandmeyer bromination[8] to bromide **2**, where subsequent reduction of the nitro group

[a] *Dr. M. Gutsche, Dr. D. Pfaff, Prof. Dr. J. Podlech*
Institut für Organische Chemie
Karlsruher Institut für Technologie (KIT)
Kaiserstraße 12
76131 Karlsruhe (Germany)
E-mail: joachim.podlech@kit.edu
Homepage: http://www.ioc.kit.edu/podlech/

Supporting information for this article is available on the WWW under https://doi.org/10.1002/ejoc.202301052

Research Article
doi.org/10.1002/ejoc.202301052

furnished aniline **3** (Scheme 2).[9] The coupling partner for a Suzuki coupling, 2-(4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4a**), was obtained by halogen-metal exchange of 4-bromoanisol with butyl lithium followed by transmetalation with 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (iPrOBpin).[10] Suzuki coupling of bromide **3** and boronate **4a** could be achieved with standard conditions[11] and gave biphenyl **5** with 85% yield, which was then transferred into *ortho*-iodobiphenyl **8**.

Direct Ullmann coupling of bromide **2** yielded 2,2′-dinitrobiphenyl **6**,[12] where the excellent 87% yield is most likely due to the presence of the electron-withdrawing nitro groups.[13] These were subsequently reduced yielding diamine **7**,[14] which was subjected to a double Sandmeyer reaction furnishing 2,2′-diiodobiphenyl **9**.[14] A careful temperature control turned out to be crucial in the latter reaction: Performing the reaction in an ice/NaCl bath gave a poor 23% yield, while a significantly better yield of 44% was obtained, when the reaction was kept at −10 °C using a cryostat.

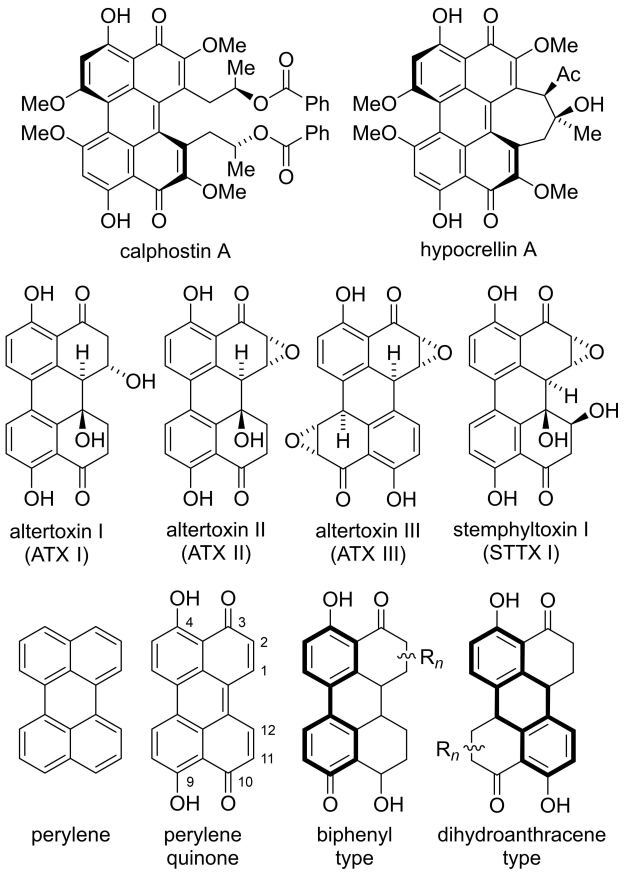


Figure 1. A selection of perylenequinone-derived natural products.

Both iodinated biphenyls **8** and **9** should be suitable precursors for the reaction with alkynes. Nevertheless, iodobiphenyl **8** could only be reacted in a test reaction with tolane (diphenylacetylene, **10**; Table 1). The published conditions [palladium(II) acetate, tetrabutylammonium chloride, and sodium acetate][15] resulted in an excellent quantitative yield for this alkyne, while no product at all was obtained, when these conditions were applied to but-2-yne-1,4-diyl diacetate (**11**) or 1,4-bis(*tert*-butyldimethylsilyloxy)but-2-yne (**12**). The protected hydroxymethyl groups, which would have been present in the aspired phenanthrenes **15** and **16**, respectively, were intended to be deprotected, oxidized to the respective aldehydes, and subjected to olefinations with subsequent reduction of the double bond to yield key intermediate **B** (see Scheme 1).

No significant improvement was achieved, when 2,2′-diiodobiphenyl **9** was reacted with tolane (**10**), with alkyne **11**, or with di-*tert*-butyl oct-4-ynedioate (**13**). In the here applied protocol we used tetrakis(triphenylphosphine)palladium(0), Xantphos as ligand, and potassium carbonate as base.[16] The test reaction with tolane yielded an impure product, which could not be purified, and reactions with alkynes **11** and **13** resulted either in a poor 15% yield or furnished no product at all (Table 1).

In the course of our investigations,[17] it turned out that the methoxy group is not ideal and the respective intermediates occasionally show insufficient solubilities. Hexyloxy-substituted substrates proved to be better suited and were (partly in parallel to the still used methoxy group) mostly used in the due course. A further attempt following the [4 + 2] approach should exert a biphenyl *ortho*-carboxylic acid **24**, which was made accessible by protection[18] and bromination[19] of 3-hydroxybenzaldehyde (**18**), and intermediately converting the carbaldehyde group furnishing acetal **21** (Scheme 3). Suzuki coupling[20] with boronate **4b** (synthesized from phenol in 3 steps, depicted in Scheme 2) yielded biphenyl derivative **22**, which was cleaved[21]

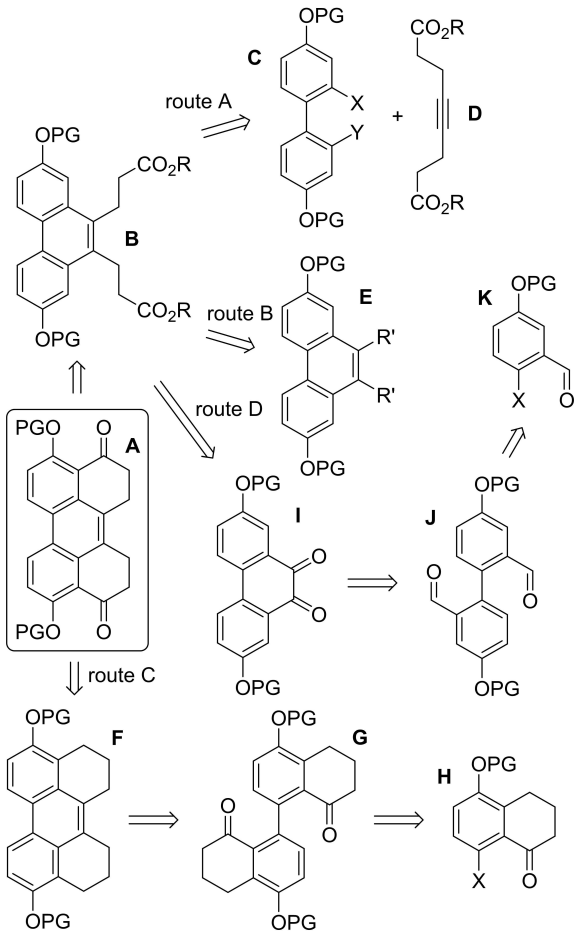
Table 1. [4 + 2] approach to phenanthrene derivatives.

Biphenyl	Alkyne, R	Conditions	Phenanthrene (Yield)
8	**10**, Ph	$Pd(OAc)_2$, Bu_4NCl, NaOAc, DMF, 100 °C, 66 h	**14** (quant.)
8	**11**, CH_2OAc	$Pd(OAc)_2$, Bu_4NCl, NaOAc, DMF, 100 °C, 24 h	**15** (–)
8	**12**, $CH_2OTBDMS$	$Pd(OAc)_2$, Bu_4NCl, NaOAc, DMF, 100 °C, 66 h	**16** (–)
9	**10**, Ph	$PdCl_2(PPh_3)_2$, Xantphos, K_2CO_3, toluene, 120 °C, 65 h	**14** ([a])
9	**13**, $(CH_2)_2CO_2tBu$	$Pd(PPh_3)_4$, Xantphos, K_2CO_3, toluene, 120 °C, 78 h	**17a** (15%)
9	**13**, $(CH_2)_2CO_2tBu$	$Pd(PPh_3)_4$, Xantphos, K_2CO_3, toluene, 150 °C, 78 h	**17a** (15%)
9	**11**, CH_2OAc	$PdCl_2(PPh_3)_2$, Xantphos, K_2CO_3, toluene, 120 °C, 65 h	**15** (–)
24	**13**, $(CH_2)_2CO_2tBu$	$Pd(OAc)_2$, acridine, Ag_2CO_3, DMF, 140 °C, 18 h	**17b** (5%)

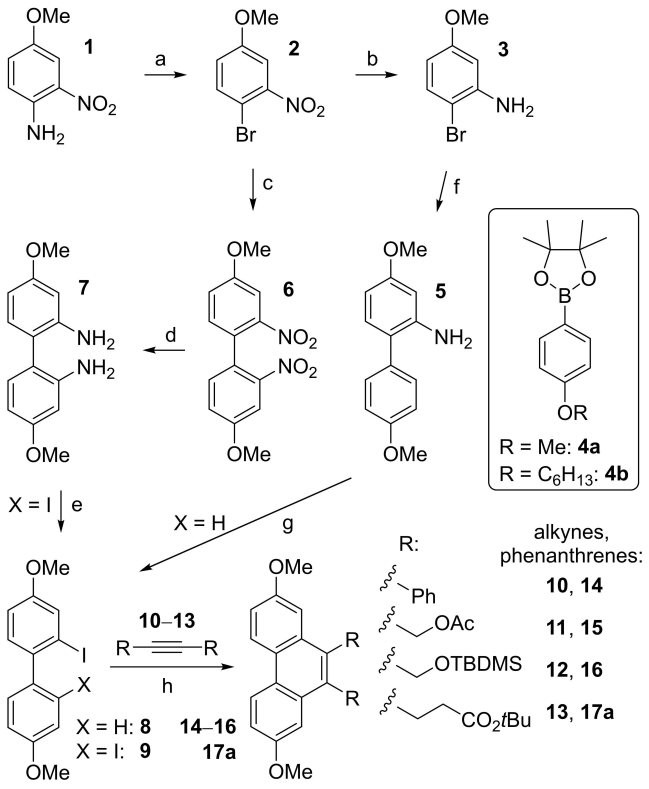
[a] The product contained impurities which could not be removed.

Research Article
doi.org/10.1002/ejoc.202301052

Chemistry Europe
European Chemical Societies Publishing



Scheme 1. Retrosynthesis for the framework of biphenyl-type perylene-derived mycotoxins.

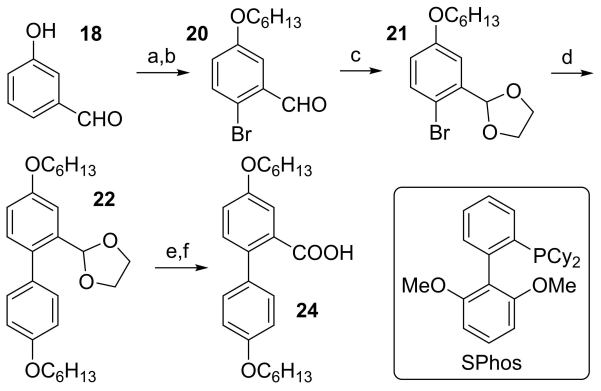


Scheme 2. [4 + 2] approach to phenanthrene derivatives. Conditions: a) $NaNO_2$, HBr (48%), MeCN, 0 °C→rt, 2 h, then CuBr, HBr (48%), 80 °C, 0.5 h, 75%; b) Fe, NH_4Cl, EtOH/H_2O (3:2), 90 °C, 1 h, 94%; c) act. Cu, DMF, 170 °C, 3 h, 87%; d) H_2, Pd/C, EtOAc, rt, 45 h, 92%; e) $NaNO_2$, conc. HCl, MeCN, −10 °C, 1 h, then KI, 0→80 °C, 20 h, 44%; f) **4a**, cat. $Pd(PPh_3)_4$, K_2CO_3, toluene/H_2O/EtOH (3:2:1), 100 °C, 21 h, 85%; g) $NaNO_2$, 4 M HCl, THF/H_2O (1:2), 0 °C, 1.5 h, then KI, 0 °C→rt, 18 h, 68%; h) see Table 1.

to liberate the aldehyde function and oxidized in a Krauss oxidation.[22] Nevertheless, coupling of biphenylcarboxylic acid **24** with alkyne **13** using palladium(II) acetate as catalyst and acridine as ligand[23] furnished a more than disappointing 5% yield of adduct **17b**. Further tested methods following route A turned out to be similarly unsuccessful; the respective investigations are not included herein. This approach was consequently not further pursued.

Route B required the synthesis and modification of phenanthrene derivatives. We started with 3-hydroxyacetophenone **25** and attached a hexyl protecting group (Scheme 4).[24] 3-Methoxyacetophenone could be purchased and was used similar as the respective hexyloxyacetophenone **26b**. Bromination with *N*-bromosuccinimide (NBS) and iodine furnished 2-bromoacetophenones **27**,[25] which were coupled in Ullmann reactions to yield diacylbiphenyls **28**.[12] For all Ullmann couplings described herein we used freshly activated copper powder, where the copper was treated with iodine and then with acetone and concentrated hydrochloric acid.[12]

For the olefination we scheduled a McMurry reaction, where the first test reaction was performed with the methoxy derivative **28a**. Reaction with titanium(IV) chloride and zinc[26] gave the desired phenanthrene **30a** only with a poor 4% yield

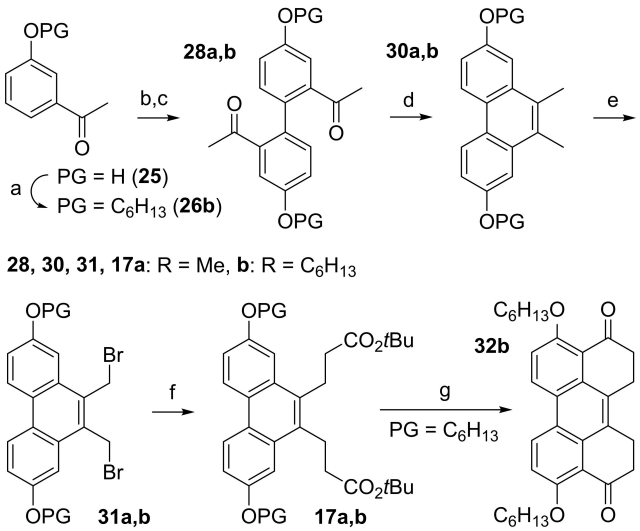


Scheme 3. Synthesis of biphenylcarboxylic acid **24**. Conditions: a) $C_6H_{13}Br$, K_2CO_3, DMF, 80 °C, 18 h, (→**19**), quant.; b) Br_2, AcOH, rt, 48 h, 86%; c) glycol, TosOH, toluene, reflux, Dean-Stark trap, 24 h, 67%; d) **4b**, cat. $Pd(OAc)_2$, SPhos, Cs_2CO_3, dioxane/H_2O (6:1), 70 °C, 17 h, 78%; e) 5% HCl, THF, rt, 24 h, (→**23**), 92%; f) $NaClO_2$, NaH_2PO_4, isobutene, *t*BuOH/THF/H_2O (4:2:1), rt, 18 h, 91%.

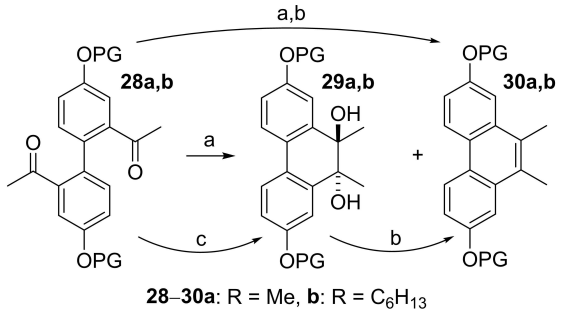
together with 68% of the pinacol coupling product **29a** (Scheme 5, central reaction arrow).[27] The resulting mixture, mainly consisting of pinacol **29a**, was reduced with triethylsilane[28] to phenanthrene **30a**, where a yield of 58% (two steps) was achieved (reaction sequence given on top of

Research Article
doi.org/10.1002/ejoc.202301052

Chemistry Europe
European Chemical Societies Publishing



Scheme 4. Olefination approach to phenanthrene derivatives. Conditions: a) $C_6H_{13}Br$, K_2CO_3, DMF, 90 °C, 18 h, 78%; b) NBS, I_2, MeCN, rt, 18 h (PG = Me, **27a**: 95%; PG = C_6H_{13}, **27b**: 69%); c) act. Cu, DMF, 175 °C, 16 h (52%, 51%, resp.); d) details are given in Scheme 5; e) NBS, AIBN, CCl_4, 90 °C, 18 h (94%, 80%); f) *t*BuOAc, LDA, THF, −78 °C, 1.5 h, then **31a,b**, THF, −78 °C→rt, 17 h (74%, 84%); g) P_2O_5 in $MeSO_3H$, 60 °C, 3 h, 74%.



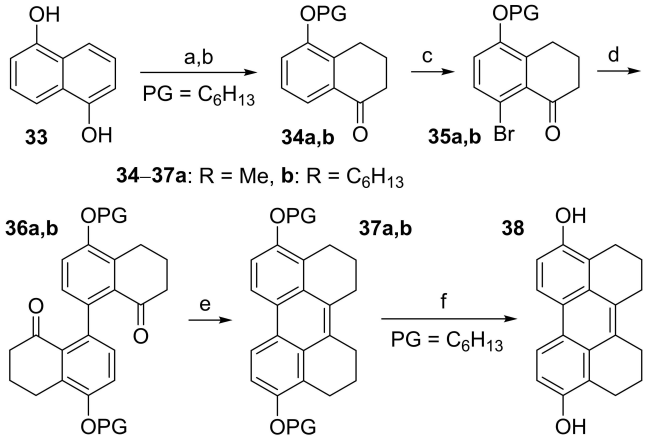
Scheme 5. Olefination of diacetylated biphenyls. Conditions: a) Zn, $TiCl_4$, pyridine, reflux, 18 h (PG = Me, **29a**: 68%, **30a**: 4%); b) Et_3SiH, $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C→rt, 1 h, [PG = Me, **30a**: 58% (2 steps from **28a**); 95% (from **29a**); PG = C_6H_{13}, **30b**: 90% (from **29b**)]; c) Zn, $ZnCl_2$, THF/H_2O (1:1), rt, 3 h (PG = Me, **29a**: 98%; PG = C_6H_{13}, **29b**: 85%).

Scheme 5). Nevertheless, best results were obtained, when we directly aimed for a pinacol coupling using zinc together with zinc chloride[29] and then reduced the diol with triethylsilane to phenanthrene **30**. Yields of 95% (PG = Me) and 77% (PG = C_6H_{13}), respectively, were here obtained over two steps. It could be noted that the NMR spectra of **29** showed signals of only one diastereoisomer. A Corey-Winter reaction, which would require a *cis* arrangement of the hydroxy groups,[30] was not successful, giving some evidence for the *trans* arrangement in diols **29**. Further evidence in this regard came from findings described in the text to Scheme 8 (*vide infra*).

9,10-Dimethylphenanthrenes **30** were doubly brominated in a Wohl-Ziegler bromination with NBS and azobis(isobutyronitrile) (AIBN) as radical starter.[31] The resulting dibromides **31** were reacted with the lithium enolate of *tert*-butyl acetate, yielding diesters **17** with good yields.[31] They were subjected to double Friedel-Crafts acylations aiming for pentacycles **32**, where we used Eaton's reagent, i.e., a solution of phosphorus pentoxide in methanesulfonic acid, as activating agent.[33] However, the latter reaction was only successful with hexyl-protected derivative **17b**; methoxy derivative **17a** showed a poor solubility preventing clean cyclization.

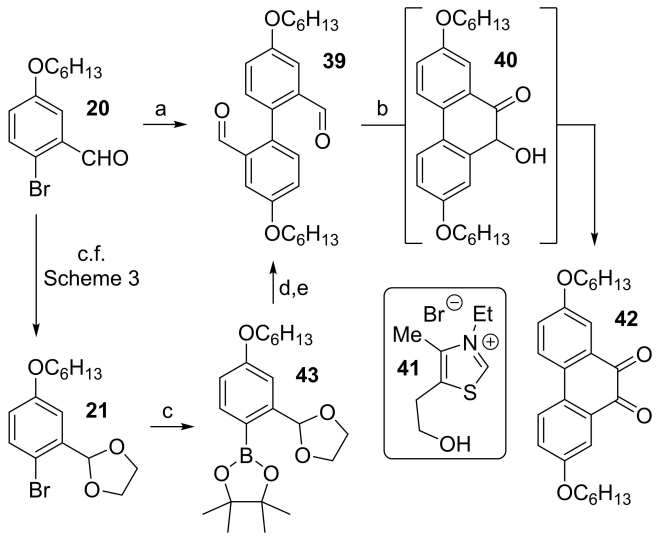
Route C (Scheme 1) was planned around a McMurry reaction installing the pentacyclic core. For this we started with commercially available 1,4-dihydroxynaphthalene (**33**), which was partially hydrogenated to 5-hydroxytetralone and protected with the hexyl group (Scheme 6).[17] The respective methyl-protected derivative **34a** could be purchased and the further sequence was followed with both protecting groups. We used the proven sequence (*vide supra*), where protected tetralones **34** were brominated with NBS, coupled in Ullmann reactions, and subjected to olefinations. The McMurry reaction turned out to work well in this case and furnished pentacycles **37** with 63 and 81%, respectively. Here we proved that the hexyl group is easily removed to deliver the unprotected hydroxylated perylene derivative **38**. This was achieved with boron tribromide[34] with 95% yield. This reagent is thus not only suitable for the cleavage of methoxy but similarly for hexyloxy groups derived from phenols. First attempts to oxidize the benzylic positions in tetracycle **37b** and to create an alternative access to dicarbonyl **32b** unfortunately turned out to be unsuccessful with a variety of tested oxidizing agents [e.g., chromium trioxide, potassium permanganate, 2-iodoxybenzoic acid (IBX), or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)]. Apparently, **37b** contains too many reactive positions to easily achieve a clean oxidation at this stage.

We followed a further route to diol **29b** via the respective phenanthrenequinone **42** (Scheme 7, route D). Here we started with the already mentioned bromobenzaldehyde **20** (see Scheme 3) which was coupled in an Ullmann reaction to yield dialdehyde **39**. Unfortunately, this coupling furnished the product with a side product, which could neither be identified nor separated by chromatography. We thus used a somewhat



Scheme 6. McMurry approach from binaphthyl derivatives. Conditions: a) H_2 (6 bar), cat. Pd/C, aq. NaOH, iPrOH, 70 °C, 14.5 h; b) $C_6H_{13}Br$, K_2CO_3, acetone, reflux, 7 h, 74% (2 steps); c) NBS, MeCN, rt, 24 h, (PG = Me, **35a**: 98%; PG = C_6H_{13}, **35b**: 91%); d) act. Cu, DMF, reflux, 3 h, (PG = Me, **36a**: 63%; PG = C_6H_{13}, **36b**: 96%); e) Zn, $TiCl_4$, pyridine, THF, reflux, 18 h, (PG = Me, **37a**: 63%, PG = C_6H_{13}, **37b**: 81%); f) BBr_3, CH_2Cl_2, 0 °C→rt, 17 h, 92%.

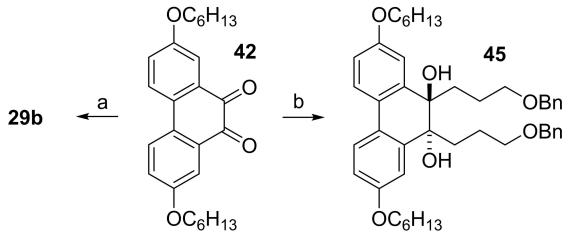
Research Article
doi.org/10.1002/ejoc.202301052



Scheme 7. Stetter approach to phenanthrene derivatives. Conditions: a) act. Cu, DMF, reflux, 3 h, 56%; b) cat. **41**, Et_3N, MeOH, reflux, 20 h, then air, MeOH/H_2O (1:4), rt, 2.5 h, quant.; c) BuLi, THF, −78 °C, 45 min, then iPrOBpin, THF, −78 °C→rt, overnight, 79%; d) **20**, $Pd(OAc)_2$, SPhos, Cs_2CO_3, dioxane/H_2O (6:1), 80 °C, 20 h (→**44**, 71%); e) 5% HCl/THF (1:2), rt, 48 h, 88%.

more laborious, but clean and easy to perform bypass: Acetal **21**, which had similarly been mentioned in Scheme 3, was transferred into boronate **43**. Suzuki coupling with bromide **20** and cleavage of the acetal finalized the alternative route to **39**. This dialdehyde could by cyclized in an intramolecular Stetter reaction using thiazolium salt **41** as catalyst,[35] presumably yielding acyloin **40**, which was immediately oxidized by purging with oxygen (air) to furnish diketone **42**.

Addition of a methyl Grignard reagent to diketone **42** yielded the same diastereoisomer of pinacol **29b**, which has already been obtained previously (Scheme 8). Since it has been noted by Criegee et al. that nucleophilic additions to phenanthrene-9,10-quinones exclusively yield *trans* products,[36] we are quite convinced that all routes to **29** (either from **28** or from **42**) yield a *trans* product. The addition of 3-benzyloxypropyl magnesium bromide to diketone **42** was similarly successful and delivered diol **45** with 78% yield. Anyway, this route, which in the further course would require debenzylation, oxidation, and Friedel-Crafts acylation, was no longer followed, since the respective products **32** were obtained in the meantime by the route described in Scheme 4.



Scheme 8. Grignard additions to phenanthrene-9,10-dione **42**. Conditions: a) MeMgI, THF/Et_2O (1:1), reflux, 2 h, 64%; b) $BnO(CH_2)_3MgBr$, THF, reflux, 15 h, 79%.

Conclusions

We successfully completed the synthesis of the frameworks of altertoxin I and the related mycotoxins. A 7-step synthesis from 3-hydroxyacetophenone furnished the dicarbonyl framework, while a 5-step sequence starting from 1,5-dihydroxynaphthalene led to the respective decarbonylated core. Further attempts to synthesized these structures turned out to be not successful, but made a number of interesting intermediates accessible, which should be useful for other synthetic endeavors. Work in direction of the final perylenequinone-derived natural products is ongoing in our laboratories.

Experimental Section

1,1′-{4,4′-Bis(hexyloxy)-[1,1′-biphenyl]-2,2′-diyl}bis(ethan-1-one) (28b): Based on a published protocol,[12] a solution of bromide **27b** (3.00 g, 10.0 mmol) in anhydrous DMF (10 mL) was added dropwise under an argon atmosphere to a slurry of freshly activated Cu powder (2.54 g, 40.0 mmol) in anhydrous DMF (40 mL). The mixture was heated to 175 °C for 20 h, cooled to rt, filtered over Celite, and rinsed with EtOAc (100 mL). The filtrate was washed with H_2O (4×100 mL) and brine (100 mL), dried (Na_2SO_4), and purified by column chromatography (silica gel, *n*-hexane/EtOAc 9:1) to yield **28b** as a brown oil (1.11 g, 2.53 mmol, 51%). R_f = 0.53 (*n*-hexane/EtOAc 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89–0.95 (m, 6 H, 2×6′-H_3), 1.31–1.40 (m, 8 H, 2×4′-H_2, 2×5′-H_2), 1.43–1.52 (m, 4 H, 2×3′-H_2), 1.76–1.85 (m, 4 H, 2×2′-H_2), 2.17 (s, 6 H, 2×CH_3), 4.01 (t, ^3J = 6.5 Hz, 4 H, 2×1′-H_2), 6.98 (dd, ^3J = 8.4 Hz, ^4J = 2.7 Hz, 2 H, 2×H_{ar}), 7.06 (d, ^3J = 8.4 Hz, 2 H, 2×H_{ar}), 7.18 ppm (d, ^4J = 2.6 Hz, 2 H, 2×H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (2×CH_3), 22.7 (2×CH_2), 25.9 (2×CH_2), 29.3 (2×CH_2), 29.7 (2×CH_2), 31.7 (2×CH_2), 68.4 (2×CH_2), 114.2 (2×CH), 117.3 (2×CH), 132.0 (2×CH), 132.4 (2×C), 140.7 (2×C), 158.6 (2×C), 202.5 ppm (2×C); IR (ATR): $\tilde{\nu}$ = 2929 (w), 2858 (w), 1686 (m), 1601 (m), 1467 (m), 1353 (w), 1279 (m), 1209 (m), 1032 (m), 824 (w), 543 cm^{-1} (w); MS (FAB): *m/z* (%): 440 (12) $[M+2]^+$, 439 (27) $[M+1]^+$, 397 (10), 396 (32), 395 (100), 379 (49); HRMS (FAB): *m/z* calcd for $C_{28}H_{39}O_4^+$: 439.2843; found: 439.2841.

2,7-Bis(hexyloxy)-9,10-dimethyl-9,10-dihydrophenanthrene-9,10-diol (29b): Based on a published protocol,[29] THF/H_2O (1:1; 20 mL) was added to a mixture of biphenyl **28b** (1.10 g, 2.51 mmol), Zn (3.69 g, 56.4 mmol), and $ZnCl_2$ (762 mg, 5.59 mmol) and the suspension was stirred for 5.5 h at rt. The reaction was stopped by addition of 3 M aqueous HCl (20 mL) and stirring was maintained for 10 min. The mixture was filtered over Celite and the aqueous layer of the filtrate was extracted with EtOAc (3×50 mL). The combined organic layers were washed with H_2O (2×50 mL), saturated aqueous $NaHCO_3$ solution (50 mL), and brine (50 mL), dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (silica gel, *n*-hexane/EtOAc 5:1) to yield **29b** as a beige solid (940 mg, 2.13 mmol, 85%). R_f = 0.41 (*n*-hexane/EtOAc 3:1); m.p. 115–117 °C; ^{1}H NMR (400 MHz $CDCl_3$): δ = 0.91 (t, ^3J = 6.7 Hz, 6 H, 2×6'-H_3), 1.29 (s, 6 H, 2×CH_3), 1.32–1.42 (m, 8 H, 2×4'-H_2, 2×5'-H_2), 1.44–1.54 (m, 4 H, 2×3'-H_2), 1.80 (tt, ^3J = 6.9 Hz, ^3J = 7.3 Hz, 4 H, 2×2'-H_2), 2.17 (bs, 2 H, 2×OH), 4.02 (m, 4 H, 2×1'-H_2), 6.84 (dd, ^3J = 8.5 Hz, ^4J = 2.5 Hz, 2 H, 3-H, 6-H), 7.22 (d, ^4J = 2.5 Hz, 2 H, 1-H, 8-H), 7.53 ppm (d, ^3J = 8.5 Hz, 2 H, 4-H, 5-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (2×CH_3), 22.8 (2×CH_3), 24.4 (2×CH_2), 25.9 (2×CH_2), 29.5 (2×CH_2), 31.8 (2×CH_2), 68.2 (2×CH_2), 77.8 (2×C), 109.8 (2×CH), 113.6 (2×CH), 124.5 (2×CH), 124.5 (2×C), 143.3 (2×C), 159.0 ppm (2×C); IR (ATR): $\tilde{\nu}$ = 3405 (br), 2927 (m), 2857 (w), 1610 (w), 1582 (w), 1467 (m), 1432 (m), 1385 (w), 1275 (m), 1240 (m), 1163 (m), 1046 (m), 946 (m), 888 (w), 799 (m), 769 (w), 735 (w), 600

(w), 497 cm^{-1} (w); MS (FAB): *m/z* (%): 441.3 (32) $[M+1]^+$, 440.3 (100) $[M]^+$, 423.2 (49) $[M–OH]^+$, 395.2 (14), 379.3 (19), 213.0 (17), 212.0 (17), 211 (24); HRMS (FAB): *m/z* calcd for $C_{28}H_{40}O_4$: 440.2921; found: 440.2922; elemental analysis calcd (%) for $C_{28}H_{40}O_4$: C 76.33, H 9.15; found: C 76.28, H 9.05.

2,7-Bis(hexyloxy)-9,10-dimethylphenanthrene (30 b): Based on a published protocol,[28] Et_3SiH (1.30 mL, 946 mg, 8.14 mmol) was added to a solution of diol **29 b** (899 mg, 2.04 mmol) in CH_2Cl_2 (20 mL). The mixture was cooled to 0 °C, stirred for 15 min and $BF_3{\cdot}OEt_2$ (1.03 mL, 1.16 g, 8.17 mmol) was added dropwise. Stirring was continued at that temperature for 1.5 h, 1 M aqueous Na_2CO_3 solution (20 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (silica gel, *n*-hexane/CH_2Cl_2 3:1) to yield **30 b** as a colorless, fluffy solid (748 mg, 1.84 mmol, 90 %). R_f = 0.44 (*n*-hexane/CH_2Cl_2 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88–0.97 (m, 6 H, 2×6′-H_3), 1.32–1.45 (m, 8 H, 2×4′-H_2, 2×5′-H_2), 1.47–1.59 (m, 4 H, 2×3′-H_2), 1.88 (quint, ^3J = 6.8 Hz, 4 H, 2×2′-H_2), 2.68 (s, 6 H, 2×CH_3), 4.13 (t, ^3J = 6.6 Hz, 4 H, 2×1′-H_2), 7.22 (dd, ^3J = 9.0 Hz, ^4J = 2.6 Hz, 2 H, 2×H_{ar}), 7.44 (d, ^4J = 2.6 Hz, 2 H, 2×H_{ar}), 8.50 ppm (d, ^3J = 9.1 Hz, 1 H, 2×H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (2×CH_3), 16.3 (2×CH_3), 22.8 (2×CH_2), 26.0 (2×CH_2), 29.6 (2×CH_2), 31.8 (2×CH_2), 68.3 (2×CH_2), 107.1 (2×CH), 115.5 (2×CH), 123.9 (2×CH), 123.9 (2×C), 129.4 (2×C), 132.6 (2×C), 157.3 ppm (2×C); IR (ATR): $\tilde{\nu}$ = 2926 (m), 2859 (m), 1608 (m), 1491 (m), 1468 (m), 1429 (m), 1378 (m), 1327 (w), 1278 (m), 1219 (s), 1079 (m), 1032 (m), 994 (m), 960 (w), 909 (w), 853 (m), 840 (m), 813 (m), 717 (w), 604 (w), 457 cm^{-1} (w); MS (FAB): *m/z* (%): 409 (39), 408 (100), 407 (23), 406 (28), 239 (14); HRMS (FAB): *m/z* calcd for $C_{28}H_{38}O_2$: 406.2866; found: 406.2865.

9,10-Bis(bromomethyl)-2,7-bis(hexyloxy)phenanthrene (31 b): Based on a published protocol,[31] NBS (897 mg, 5.04 mmol) and AIBN (21 mg, 0.13 mmol) were added under an argon atmosphere to a solution of phenanthrene **30 b** (1.00 g, 2.46 mmol) in CCl_4 (50 mL) and the mixture was heated to reflux for 4 h. Further AIBN (21 mg, 0.13 mmol) was added and heating was continued for further 12 h. The mixture was cooled to rt, concentrated at reduced pressure, purified by column chromatography (silica gel, *n*-hexane/CH_2Cl_2 4:1) to yield **31 b** as a yellow solid (1.11 g, 1.97 mmol, 80 %). R_f = 0.37 (*n*-hexane/CH_2Cl_2 2:1); R_f = 0.59 (*n*-hexane/EtOAc 9:1); m.p. 163–164 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84–0.98 (m, 6 H, 2×6′-H_3), 1.33–1.43 (m, 8 H, 2×4′-H_2, 2×5′-H_2), 1.47–1.60 (m, 4 H, 2×3′-H_2), 1.84–1.97 (m, 4 H, 2×2′-H_2), 4.17 (t, ^3J = 6.5 Hz, 4 H, 2×1′-H_2), 5.07 (s, 4 H, 2×CH_2Br), 7.31 (dd, ^3J = 9.1 Hz, ^4J = 2.5 Hz, 2 H, 2×H_{ar}), 7.52 (d, ^4J = 2.6 Hz, 2 H, 2×H_{ar}), 8.51 ppm (d, ^3J = 9.2 Hz, 2 H, 2×H_{ar}); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (2×CH_3), 22.8 (2×CH_2), 26.0 (2×CH_2), 27.3 (2×CH_2), 29.4 (2×CH_2), 31.8 (2×CH_2), 68.4 (2×CH_2), 106.4 (2×CH), 118.4 (2×CH), 124.4 (2×CH), 125.6 (2×C), 129.8 (2×C), 131.5 (2×C), 157.7 ppm (2×C); IR (ATR): $\tilde{\nu}$ = 2927 (w), 2868 (w), 1612 (m), 1493 (m), 1433 (m), 1379 (m), 1286 (w), 1233 (m), 1202 (m), 1083 (w), 1030 (m), 933 (w), 884 (w), 824 (m), 812 (m), 711 (w), 650 (m), 580 (w), 530 (w), 451 cm^{-1} (w); MS (FAB): *m/z* (%): 566.2 (57) $[M]^+$, 564.2 (100) $[M]^+$, 562.2 (52) $[M]^+$, 485.2 (29), 483.2 (29), 405.4 (38), 404.3 (81), 236.1 (48), 235.1 (33); HRMS (FAB): *m/z* calcd for $C_{28}H_{36}{}^{79}Br_2O_2$: 562.1077; found: 562.1075; elemental analysis calcd (%) for $C_{28}H_{36}Br_2O_2$: C 59.59, H 6.43; found: C 59.32, H 6.31.

Di-*tert*-butyl 3,3'-(2,7-Bis(hexyloxy)phenanthrene-9,10-diyl)dipropionate (17 b): Following a published protocol,[32] BuLi (2.5 M in hexanes; 1.02 mL, 2.55 mmol) was slowly added dropwise under an argon atmosphere to a cooled (−78 °C) solution of iPr_2NH (359 µL, 259 mg, 2.56 mmol) in anhydrous THF (10 mL) and stirring was continued for 30 min at this temperature. *t*BuOAc (345 µL, 299 mg, 1.16 mmol) was added slowly, stirring was continued for 90 min at this temperature, and a solution of phenanthrene **31 b** (480 mg, 0.850 mmol) in anhydrous THF (10 mL) was added dropwise. The mixture was stirred for 3 h while it was allowed to warm to rt. Saturated aqueous NH_4Cl solution (40 mL) was added and the aqueous layer was extracted with EtOAc (3×15 mL). The combined organic layers were dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (silica gel, cyclohexane/EtOAc 19:1) to yield **17 b** as a colorless solid (455 mg, 0.717 mmol, 84 %). R_f = 0.40 (*n*-hexane/EtOAc 9:1); m.p. 99–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88–0.95 (m, 6 H, 2×6′-H_3), 1.34–1.40 (m, 8 H, 2×4′-H_2, 2×5′-H_2), 1.45–1.56 (m, 4 H, 2×3′-H_2), 1.50 [s, 18 H, 2×C(CH_3)$_3$], 1.82–1.91 (m, 4 H, 2×2′-H_2), 2.56–2.62 (m, 4 H, 2×3″-H_2), 3.40–3.45 (m, 4 H, 2×2″-H_2), 4.13 (t, ^3J = 6.7 Hz, 4 H, 2×1′-H_2), 7.23 (dd, ^3J = 9.0 Hz, ^4J = 2.5 Hz, 2 H, H-3, H-6), 7.46 (d, ^4J = 2.5 Hz, 2 H, H-1, H-8), 8.50 ppm (d, ^3J = 9.1 Hz, 2 H, H-4, H-5); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (2×CH_3), 22.8 (2×CH_2), 24.5 (2×CH_2), 26.0 (2×CH_2), 28.3 (6×CH_3), 29.5 (2×CH_2), 31.8 (2×CH_2), 36.0 (2×CH_2), 68.3 (2×CH_2), 80.7 (2×C), 106.6 (2×CH), 116.4 (2×CH), 124.2 (2×CH), 124.6 (2×C), 131.0 (2×C), 132.7 (2×C), 157.6 (2×C), 172.5 ppm (2×C); IR (ATR): $\tilde{\nu}$ = 2930 (m), 2860 (w), 1719 (m), 1612 m), 1494 (m), 1434 (w), 1363 (m), 1298 (w), 1225 (s), 1144 (s), 1032 (m), 942 (w), 846 (m), 791 (m), 753 (w), 727 (w), 599 (w), 455 (w), 391 cm^{-1} (vw); MS (FAB): *m/z* (%): 636.4 (13) $[M+2]^+$, 635.4 (46) $[M+1]^+$, 634.4 (100) $[M]^+$, 578.4 (4), 538.4 (5), 524.4 (9), 523.4 (25), 505.4 (11), 463.4 (9), 277.0 (5), 249.0 (8), 235.0 (6); HRMS (FAB): *m/z* calcd for $C_{40}H_{58}O_6$: 634.4228; found: 634.4230.

4,9-Bis(hexyloxy)-1,2,11,12-tetrahydroperylene-3,10-dione (32 b): Based on a published protocol,[37] Eaton's reagent (7.7 % w/w P_2O_5 in $MeSO_3H$; 2 mL) was added under an argon atmosphere to diester **17 b** (25 mg, 39 µmol). The mixture was stirred vigorously at 60 °C for 3 h, poured into ice water (20 mL), and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (silica gel, *n*-hexane/EtOAc 3:1) to yield **32 b** as a reddish brown solid (14 mg, 29 µmol, 74 %). R_f = 0.23 (*n*-hexane/EtOAc 3:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88–0.95 (m, 6 H, 2×6′-H_3), 1.32–1.42 (m, 8 H, 2×4′-H_2, 2×5′-H_2), 1.51–1.61 (m, 4 H, 2×3′-H_2), 1.88–1.96 (m, 4 H, 2×2′-H_2), 2.92 (t, ^3J = 7.2 Hz, 4 H, 1-H_2, 12-H_2), 3.40 (t, ^3J = 7.2 Hz, 4 H, 2-H_2, 11-H_2), 4.21 (t, ^3J = 6.7 Hz, 4 H, 1′-H_2), 7.37 (d, ^3J = 9.3 Hz, 2 H, 5-H, 8-H), 8.69 ppm (d, ^3J = 9.1 Hz, 2 H, 6-H, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (2×CH_3), 22.7 (2×CH_2), 25.8 (2×CH_2), 26.9 (2×CH_2), 29.4 (2×CH_2), 31.8 (2×CH_2), 40.1 (2×CH_2), 70.0 (2×CH_2), 114.3 (2×CH), 117.7 (2×C), 123.0 (2×C), 129.2 (2×CH), 129.8 (2×C), 132.1 (2×C), 157.4 (2×C), 197.8 ppm (2×C); IR (ATR): $\tilde{\nu}$ = 3366 (br), 2923 (m), 2856 (m), 1682 (s) (C=O), 1576 (m), 1460 (m), 1439 (m), 1364 (m), 1248 (s), 1186 (s), 1118 (m), 1076 (s), 984 (m), 924 (w), 805 (s), 725 (w), 619 (w), 565 cm^{-1} (w); MS (FAB): *m/z* (%): 488.5 (16) $[M+2]^+$, 487.4 (43) $[M+1]^+$, 486.5 (23) $[M]^+$, 484.5 (14), 369.3 (16), 339.3 (18), 81.0 (100); HRMS (FAB): *m/z* calcd for $C_{32}H_{39}O_4$ $[M+1]$: 487.2843; found: 487.2842.

3,10-Bis(hexyloxy)-4,5,6,7,8,9-hexahydroperylene (37 b): Based on a published protocol,[26] $TiCl_4$ (4.72 ml, 8.16 g, 43.0 mmol) was added at 0 °C under an argon atmosphere to a slurry of Zn (5.63 g, 86.1 mmol) in THF (80 mL). The mixture was heated to reflux for 3 h, cooled to 0 °C, pyridine (1.73 mL, 1.69 g, 21.4 mmol) was added, and stirring was continued for 10 min at this temperature. The mixture was warmed to rt and a solution of diketone **36 b** (4.00 g, 8.15 mmol) in THF (30 mL) was added dropwise. The mixture was heated to reflux for 18 h, cooled to rt, and poured into saturated aqueous $NaHCO_3$ solution (400 mL). CH_2Cl_2 (200 mL) was added and the mixture was filtered over a Büchner funnel and rinsed with CH_2Cl_2 (3×50 mL). The aqueous layer was extracted with CH_2Cl_2 (2×150 mL) and the combined organic layers were dried (Na_2SO_4), concentrated at reduced pressure, and purified by recrystallization (*n*-hexane/EtOAc 19:1) to yield **37 b** as a pale yellow crystalline solid (3.02 g, 6.58 mmol, 81 %). R_f = 0.71 (*n*-hexane/EtOAc 9:1); m.p. 178–180 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, ^3J = 7.0 Hz, 6 H,

2×6'-H_3), 1.33–1.44 (m, 8 H, 2×4'-H_2, 2×5'-H_2), 1.49–1.57 (m, 4 H, 2×3'-H_2), 1.85 (tt, ^3J = 7.5 Hz, ^3J = 6.5 Hz, 4 H, 2×2'-H_2), 2.03 (tt, ^3J = 6.0 Hz, ^3J = 6.3 Hz, 4 H, 5-H_2, 8-H_2), 3.02 (t, ^3J = 6.3 Hz, 4 H, 4-H_2, 9-H_2 or 6-H_2, 7-H_2), 3.04 (t, ^3J = 6.1 Hz, 4 H, 6-H_2, 7-H_2 or 4-H_2, 9-H_2), 4.10 (t, ^3J = 6.5 Hz, 4 H, 2×1'-H_2), 7.19 (d, ^3J = 9.0 Hz, 2 H, 2-H, 11-H), 8.39 ppm (d, ^3J = 9.1 Hz, 2 H, 1-H, 12-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (2×CH_3), 22.5 (2×CH_2), 22.8 (2×CH_2), 23.9 (2×CH_2), 26.0 (2×CH_2), 27.8 (2×CH_2), 29.8 (2×CH_2), 31.8 (2×CH_2), 69.0 (2×CH_2), 111.8 (2×CH), 120.8 (2×CH), 123.0 (2×C), 124.1 (2×C), 129.1 (2×C), 129.1 (2×C), 153.2 ppm (2×C); IR (ATR): $\tilde{\nu}$ = 2923 (m), 2853 (m), 1596 (w), 1579 (w), 1462 (m), 1344 (w), 1251 (m), 1230 (m), 1192 (m), 1127 (m), 1070 (m), 1038 (m), 1022 (m), 977 (w), 789 (m), 726 cm^{-1} (m); MS (FAB): *m/z* (%): 459.5 (55) $[M+1]^+$, 458.5 (100) $[M]^+$, 457.5 (30) $[M-1]^+$, 374.3 (14), 373.3 (20) $[M-C_6H_{13}]^+$; HRMS (FAB): *m/z* calcd for $C_{32}H_{42}O_2$: 458.3179; found: 458.3181.

3,10-Dihydroxy-4,5,6,7,8,9-hexahydroperylene (38): Based on a published protocol,[34] BBr_3 (1 M in CH_2Cl_2; 409 µL, 409 µmol) was added under an argon atmosphere to a cooled (0 °C) solution of hexahydroperylene **37b** (50 mg, 109 µmol) in anhydrous CH_2Cl_2 (5 mL) and the mixture was stirred for 17.5 h at rt. MeOH (0.5 mL) was added and stirring was continued for 10 min. The mixture was concentrated at reduced pressure and purified by column chromatography (silica gel, *n*-hexane/EtOAc 3:1) to yield **38** as a light brown solid (29 mg, 100 µmol, 92%). R_f = 0.55 (*n*-hexane/EtOAc 1:1); ^{1}H NMR (400 MHz, THF-d_8): δ = 1.98 (tt, ^3J = 6.3 Hz, ^3J = 6.1 Hz, 4 H, 5-H_2, 8-H_2), 2.93–3.04 (m, 8 H, 4-H_2, 6-H_2 7-H_2, 9-H_2), 6.97 (d, ^3J = 8.9 Hz, 2 H, 2-H, 11-H), 8.09 (s, 2 H, 2×OH), 8.22 ppm (d, ^3J = 8.9 Hz, 2 H, 1-H, 12-H); ^{13}C NMR (100 MHz, THF-d_8): δ = 23.6 (2×CH_2), 24.8 (2×CH_2), 28.7 (2×CH_2), 115.7 (2×CH), 120.3 (2×C), 121.3 (2×CH), 124.8 (2×C), 129.4 (2×C), 129.9 (2×C), 152.2 ppm (2×C); IR (ATR): $\tilde{\nu}$ = 3251 (br), 2931 (w), 2839 (w), 1614 (w), 1585 (w), 1464 (m), 1372 (w), 1341 (w), 1304 (m), 1230 (m), 1193 (w), 1112 (w), 1058 (w), 1007 (m), 887 (w), 799 (m), 708 cm^{-1} (w); MS (EI, 180 °C): *m/z* (%): 291.3 (23) $[M+1]^+$, 290.3 (100) $[M]^+$, 289.3 (15) $[M-H]^+$; HRMS (EI): *m/z* calcd for $C_{20}H_{18}O_2$: 290.1301; found: 290.1302.

Supporting Information

The authors have cited additional references within the Supporting Information.[38–56]

Acknowledgements

We thank Inka Marten for supplying reference compounds and we gratefully acknowledge financial support from the Deutsche Forschungsgemeinschaft (DFG, PO 463/16-1). Open Access funding enabled and organized by Projekt DEAL.

Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: biaryls · McMurry olefination · mycotoxins · perylenequinones · total synthesis

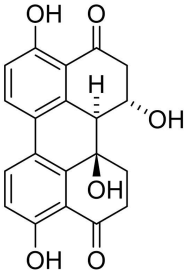
[1] a) E. Kobayashi, K. Ando, H. Nakano, T. Tamaoki, *J. Antibiot.* **1989**, *42*, 153–155; b) E. Kobayashi, K. Ando, H. Nakano, T. Iida, H. Ohno, M. Morimoto, T. Tamaoki, *J. Antibiot.* **1989**, *42*, 1470–1474; c) T. Iida, E. Kobayashi, M. Yoshida, H. Sano, *J. Antibiot.* **1989**, *42*, 1475–1481.
[2] C. Wei-Shin, C. Yuan-Teng, W. Xiang-Yi, E. Friedrichs, H. Puff, E. Breitmaier, *Liebigs Ann. Chem.* **1981**, 1880–1885.
[3] a) C. A. Broka, *Tetrahedron Lett.* **1991**, *32*, 859–862; b) F. M. Hauser, D. Sengupta, S. A. Corlett, *J. Org. Chem.* **1994**, *59*, 1967–1969; c) R. S. Coleman, E. B. Grant, *J. Am. Chem. Soc.* **1994**, *116*, 8795–8796; d) R. S. Coleman, E. B. Grant, *J. Am. Chem. Soc.* **1995**, *117*, 10889–10904; e) C. A. Merlic, C. C. Aldrich, J. Albaneze-Walker, A. Saghatelian, *J. Am. Chem. Soc.* **2000**, *122*, 3224–3225; f) C. A. Merlic, C. C. Aldrich, J. Albaneze-Walker, A. Saghatelian, J. Mammen, *J. Org. Chem.* **2001**, *66*, 1297–1309; g) E. M. O'Brien, B. J. Morgan, M. C. Kozlowski, *Angew. Chem.* **2008**, *120*, 6983–6986; *Angew. Chem. Int. Ed.* **2008**, *47*, 6877–6880; h) E. M. O'Brien, B. J. Morgan, C. A. Mulrooney, P. J. Carroll, M. C. Kozlowski, *J. Org. Chem.* **2010**, *75*, 57–68; i) B. J. Morgan, C. A. Mulrooney, E. M. O'Brien, M. C. Kozlowski, *J. Org. Chem.* **2010**, *75*, 30–43; j) B. J. Morgan, C. A. Mulrooney, M. C. Kozlowski, *J. Org. Chem.* **2010**, *75*, 44–56.
[4] K. Steingröver, PhD thesis, Universität-Gesamthochschule Paderborn (Germany), **2001**.
[5] J. Podlech, S. C. Fleck, M. Metzler, J. Bürck, A. S. Ulrich, *Chem. Eur. J.* **2014**, *20*, 11463–11470.
[6] R. Geris, M. A. Pinho, E. F. Boffo, T. J. Simpson, *J. Nat. Prod.* **2022**, *85*, 2236–2250.
[7] M. Gutsche, J. Podlech, *Eur. J. Org. Chem.* **2023**, ejoc.202301053.
[8] K. Tsuchiya, K. Sakaguchi, H. Kasuga, A. Kawakami, H. Taka, H. Kita, K. Ogino, *Polymer* **2010**, *51*, 616–622.
[9] C. Kong, T. G. Driver, *Org. Lett.* **2015**, *17*, 802–805.
[10] M. Y. Jo, S. S. Park, J. H. Kim, *Synth. Met.* **2012**, *162*, 70–78.
[11] A. Baccalini, S. Vergura, P. Dolui, S. Maiti, S. Dutta, S. Maity, F. F. Khan, G. K. Lahiri, G. Zanoni, D. Maiti, *Org. Lett.* **2019**, *21*, 8842–8846.
[12] R. Holzwarth, R. Bartsch, Z. Cherkaoui, G. Solladié, *Chem. Eur. J.* **2004**, *10*, 3931–3935.
[13] J. Lindley, *Tetrahedron* **1984**, *40*, 1433–1456.
[14] C.-L. Deng, S. C. K. Hau, X.-S. Peng, H. N. C. Wong, *Synlett* **2016**, *27*, 2095–2100.
[15] R. C. Larock, M. J. Doty, Q. Tian, J. M. Zenner, *J. Org. Chem.* **1997**, *62*, 7536–7537.
[16] J. Ma, G. Li, Y. Qiao, J. Tu, S. Liu, F. Xu, *Synlett* **2015**, *26*, 1991–1996.
[17] O. Geiseler, M. Müller, J. Podlech, *Tetrahedron* **2013**, *69*, 3683–3689.
[18] J. Y. Hwang, L. A. Arnold, F. Zhu, A. Kosinski, T. J. Mangano, V. Setola, B. L. Roth, R. K. Guy, *J. Med. Chem.* **2009**, *52*, 3892–3901.
[19] N. Negoro, S. Sasaki, M. Ito, S. Kitamura, Y. Tsujihata, R. Ito, M. Suzuki, K. Takeuchi, N. Suzuki, J. Miyazaki, T. Santou, T. Odani, N. Kanzaki, M. Funami, T. Tanaka, T. Yasuma, Y. Momose, *J. Med. Chem.* **2012**, *55*, 1538–1552.
[20] M. Altemöller, T. Gehring, J. Cudaj, J. Podlech, H. Goesmann, C. Feldmann, A. Rothenberger, *Eur. J. Org. Chem.* **2009**, 2130–2140.
[21] P. A. Grieco, M. Nishizawa, T. Oguri, S. D. Burke, N. Marinovic, *J. Am. Chem. Soc.* **1977**, *99*, 5773–5780.
[22] M. Ohashi, K. Gamo, Y. Tanaka, M. Waki, Y. Beniyama, K. Matsuno, J. Wada, M. Tenta, J. Eguchi, M. Makishima, N. Matsuura, T. Oyama, H. Miyachi, *Eur. J. Med. Chem.* **2015**, *90*, 53–67.
[23] C. Wang, S. Rakshit, F. Glorius, *J. Am. Chem. Soc.* **2010**, *132*, 14006–14008.
[24] A. Tourteau, V. Andrzejak, M. Body-Malapel, L. Lemaire, A. Lemoine, R. Mansouri, M. Djouina, N. Renault, J. El Bakali, P. Desreumaux, G. G. Muccioli, D. M. Lambert, P. Chavatte, B. Rigo, N. Leleu-Chavain, R. Millet, *Bioorg. Med. Chem.* **2013**, *21*, 5383–5394.
[25] M. Kreibich, M. Gemander, D. Peter, D. B. Yadav, C. B. de Koning, M. A. Fernandes, I. R. Green, W. A. L. van Otterlo, R. Brückner, *Eur. J. Org. Chem.* **2020**, 2929–2955.
[26] M. Oelgemöller, R. Frank, P. Lemmen, D. Lenoir, J. Lex, Y. Inoue, *Tetrahedron* **2012**, *68*, 4048–4056.
[27] a) A. Gansäuer, *Chem. Commun.* **1997**, 457–458; b) T. Li, W. Cui, J. Liu, J. Zhao, Z. Wang, *Chem. Commun.* **2000**, 139–140.
[28] G. C. Vougioukalakis, M. Orfanopoulos, *Tetrahedron Lett.* **2003**, *44*, 8649–8652.
[29] M. M. Hossain, K. Thakur, M. R. Talipov, S. V. Lindeman, S. Mirzaei, R. Rathore, *Org. Lett.* **2021**, *23*, 5170–5174.

[30] a) E. J. Corey, F. A. Carey, R. A. E. Winter, *J. Am. Chem. Soc.* **1965**, *87*, 934–935; b) J. H. Rigby, B. Bazin, J. H. Meyer, F. Mohammadi, *Org. Lett.* **2002**, *4*, 799–801.
[31] S. Hauptmann, *Chem. Ber.* **1960**, *93*, 2604–2612.
[32] T. von Hirschheydt, V. Wolfart, R. Gleiter, H. Irngartinger, T. Oeser, F. Rominger, F. Eisenträger, *J. Chem. Soc. Perkin Trans. 2* **2000**, 175–183.
[33] P. E. Eaton, G. R. Carlson, J. T. Lee, *J. Org. Chem.* **1973**, *38*, 4071–4073.
[34] K. Koch, J. Podlech, E. Pfeiffer, M. Metzler, *J. Org. Chem.* **2005**, *70*, 3275–3276.
[35] F. Dallacker, H. Leidig, *Chem. Ber.* **1979**, *112*, 2672–2679.
[36] R. Criegee, E. Höger, G. Huber, P. Kruck, F. Marktscheffel, H. Schellenberger, *Justus Liebigs Ann. Chem.* **1956**, *599*, 81–125.
[37] D. Zewge, C.-y. Chen, C. Deer, P. G. Dormer, D. L. Hughes, *J. Org. Chem.* **2007**, *72*, 4276–4279.
[38] J. L. Hartwell, *Org. Synth. Coll. Vol.* **1955**, *3*, 185; *Org. Synth.* **1944**, *24*, 22.
[39] W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923–2925.
[40] D. Qiu, Z. Zheng, F. Mo, Y. Zhang, J. Wang, *Can. J. Chem.* **2012**, *90*, 71–74.
[41] O. Geiseler, J. Podlech, *Tetrahedron* **2012**, *68*, 7280–7287.
[42] E. Zysman-Colman, K. Arias, J. S. Siegel, *Can. J. Chem.* **2009**, *87*, 440–447.
[43] H.-R. Bjørsvik, R. R. González, L. Liguori, *J. Org. Chem.* **2004**, *69*, 7720–7727.
[44] T. Chatterjee, G.-b. Roh, M. A. Shoaib, C.-H. Suhl, J. S. Kim, C.-G. Cho, E. J. Cho, *Org. Lett.* **2017**, *19*, 1906–1909.
[45] D. Zhu, Q. Liu, B. Luo, M. Chen, R. Pi, P. Huang, S. Wen, *Adv. Synth. Catal.* **2013**, *355*, 2172–2178.
[46] C. Zhu, D. Wang, D. Wang, Y. Zhao, W.-Y. Sun, Z. Shi, *Angew. Chem.* **2018**, *130*, 8986–8991; *Angew. Chem. Int. Ed.* **2018**, *57*, 8848–8853.
[47] G. Hirata, N. Yamada, S. Sanada, G. Onodera, M. Kimura, *Org. Lett.* **2015**, *17*, 600–603.
[48] C. Yang, Z.-L. Xu, H. Shao, X.-Q. Mou, J. Wang, S.-H. Wang, *Org. Lett.* **2015**, *17*, 5288–5291.
[49] P. A. Wender, N. M. Deschamps, T. J. Williams, *Angew. Chem.* **2004**, *116*, 3138–3141; *Angew. Chem. Int. Ed.* **2004**, *43*, 3076–3079.
[50] R. G. Iafe, J. L. Kuo, D. G. Hochstatter, T. Saga, J. W. Turner, C. A. Merlic, *Org. Lett.* **2013**, *15*, 582–585.
[51] G. R. Stephenson, C. E. Anson, A. V. Malkov, C. Roe, *Eur. J. Org. Chem.* **2012**, 4716–4732.
[52] F. Liu, G. Zhao, W. Cai, D. Xu, B. Zhao, *Org. Biomol. Chem.* **2018**, *16*, 7498–7502.
[53] J. D. Genzer, G. A. Conrad (Warner-Lambert Company), DE 2219116 A, **1972**; *Chem. Abstr.* **1973**, *78*, 43137.
[54] A. Latorre, A. Urbano, M. C. Carreño, *Chem. Commun.* **2009**, 6652–6654.
[55] M.-Y. Chang, T.-W. Lee, M.-H. Wu, *Org. Lett.* **2012**, *14*, 2198–2201.
[56] K. J. Frankowski, J. E. Golden, Y. Zeng, Y. Lei, J. Aubé, *J. Am. Chem. Soc.* **2008**, *130*, 6018–6024.

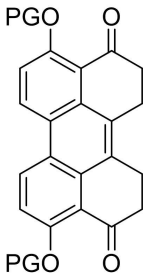
Manuscript received: October 13, 2023
Revised manuscript received: November 20, 2023
Accepted manuscript online: November 20, 2023
Version of record online: ■■, ■■

RESEARCH ARTICLE

The core of the perylenequinone-derived mycotoxin altertoxin I was synthesized either from 3-hydroxyacetophenone or from 1,5-dihydroxynaphthalene, where Suzuki couplings, Ullmann couplings, McMurry olefinations, and Friedel-Crafts acetylation were key steps in the respective syntheses.



altertoxin I
(ATX I)



*Dr. M. Gutsche, Dr. D. Pfaff, Prof. Dr. J. Podlech**