A Novel Strategy for the Synthesis of Oxygenated Phenanthrenes Involving a Combination of Ullmann and McMurry Reactions

Anne-Elisabeth Gies and Michel Pfeffer*

Laboratoire de Synthèses Métallo-Induites, UMR 7513 CNRS, Université Louis Pasteur, 4 rue Blaise Pascal, 67070 Strasbourg, France

Received December 29, 1998

A general synthetic procedure for the preparation of polyoxygenated phenanthrenes from substituted derivatives of benzaldehyde is described. The key compound is a 6,6′-biphenyl-1,1′-dicarboxaldehyde intermediate formed through an ambient temperature Ullmann coupling. The subsequent McMurry condensation gave rise to the phenanthrene in 45−57% yields.

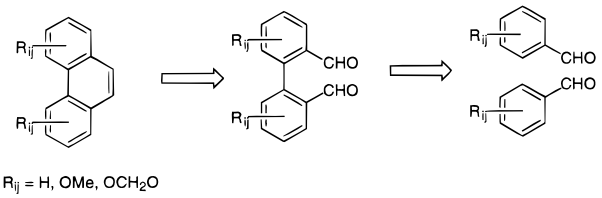
Introduction

For some years we have been interested in the palladium-induced synthesis of nitrogen heterocycles.[1] In this context, we recently studied the formation of compounds which have structural analogy with the known Aporphine family of alkaloids. [1c]

Natural aporphines are phenanthrene-based heterocycles with an original substitution pattern of hydroxyl, methoxy, and methylenedioxy groups.[2] Given their numerous biological and therapeutic properties, many efforts have focused on developing synthetic methods toward this class of compounds.[3] Our own strategy is based on the insertion of a disubstituted alkyne in the carbon−palladium bond of a 9-aminophenanthrene cyclopalladated complex.[1c] The extension of this methodology to the preparation of natural product analogues required a synthetically viable route to appropriately substituted phenanthrene precursors, prior to the final palladium-mediated step.

Despite the occurrence of the phenanthrene skeleton in many natural products[4a−c] and the biological properties[4d,e] of these compounds, many of the reported synthetic pathways to these polycylic aromatic hydrocarbons are unsatisfactory.[5] The classical obvious route utilizing a Pschorr ring closure of stilbenes[6a,b] is usually poor yielding (less than 10%). A more commonly used method involves the oxidative photochemical ring closure of stilbenes;[6c−e] however, it has many drawbacks such as a limited success on a multigram scale and a lack of selectivity, yielding mixtures of isomers. Pathways employing a precursor other than stilbene require harsh conditions[7a−c] such as strong mineral acids and are often restricted in terms of the substitution pattern.[7d,e] Moreover the requisite starting materials are often not readily available.[7f,g]

Scheme 1



In this paper, we propose an unprecedented retrosynthetic approach toward the phenanthrene nucleus [Scheme 1]. It highlights the possibility of building the C(9)−C(10) double bond during the last step of the process from a suitably preformed biaryl. Formation of the latter was achieved in a copper-mediated Ullmann aryl−aryl coupling reaction. An obvious solution for the final step led us to a novel application of the McMurry low valent titanium (LVT) intramolecular condensation of 6,6′-biphenyl-1,1′-dicarboxaldehydes (bisbenzaldehydes).

Results and Discussion

Some years ago a modified ambient temperature Ullmann-type protocol was disclosed[8] which afforded good yields of bisbenzaldehydes under very mild experimental conditions.[9] Moreover, the methodology was compatible with polyoxygenated substrates[10a] leading for instance to **2a**. Following this procedure we obtained the com-

(1) (a) Pfeffer, M. *Recl. Trav. Chem. Pays-Bas* **1990**, *109*, 567−576. (b) Pfeffer, M. *Pure Appl. Chem.* **1992**, *64*, 335−342. (c) Pfeffer, M., Beydoun, N. *Synthesis* **1990**, 729−732. (c) Pfeffer, M.; Sutter-Beydoun, N.; de Cian, A.; Fischer, J. *J. Organomet. Chem.* **1993**, *453*, 139−146. (d) Spencer, J.; Pfeffer, M. *Advances in Metal−Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: London, 1998; Vol. 6, pp 103−144.

(2) For general and updated information about the aporphines: Guinaudeau, H.; Leboeuf, M.; Cavé, A. *Lloydia* **1975**, *38*, 275−338 and references cited. (b) **1979**, *42*, 325−360; (c) **1983**, *46*, 761−835; (d) **1988**, *51*, 389−474; (e) **1994**, *57*, 1033−1135. See also, ref 3.

(3) Southon, I. W.; Buckingham, J. *Dictionary of Alkaloids*; Chapman and Hall: New York, 1989.

(4) (a) Leong, Y. W.; Kang, C. C.; Harrison, L. J.; Powell, A. D. *Phytochem.* **1997**, *44*, 157−165. (b) Majumder, P. L.; Banerjee, S.; Sen, S. *Phytochem.* **1996**, *42*, 847−852. (c) Adam, K. P.; Becker, H. *Phytochem.* **1994**, *35*, 139−143. (d) Castedo, L.; Tojo, G. *The Alkaloids, Chemistry and Physiology*, Vol. XXXIX, Chapter III (Phenanthrene alkaloids); Academic Press: San Diego, 1990. (e) Kende, A. S.; Curran, D. P. *J. Am. Chem. Soc.* **1979**, *101*, 1857−1864.

(5) For a general review, see: Floyd, A. J.; Dyke, S. F.; Ward, S. E. *Chem. Rev.* **1976**, *76*, 509−562.

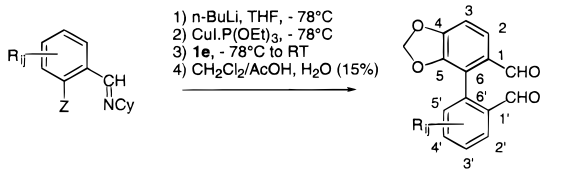
(6) (a) Wassmundt, F. W.; Kiesman, W. F. *J. Org. Chem.* **1995**, *60*, 196−201 and cited references. (b) Roblot, F.; Hocquemiller, R.; Cavé, A. *Bull. Soc. Chim. Fr.* **1990**, *127*, 258−267. (c) Mallory, F. B.; Mallory, C. *Org. React.* **1984**, *30*, 1−456. (d) Liu, L.; Yang, B.; Katz, T. J.; Poindexter, M. K. *J. Org. Chem.* **1991**, *56*, 3769−3775. (e) Grimme, S.; Pischel, I.; Nieger, M.; Vogtle, F. *J. Chem. Soc., Perkin Trans. 2* **1996**, 2771−2774.

(7) (a) Rahman, A. U.; Vuano, B. M.; Rodriguez, N. M. *Aust. J. Chem.* **1972**, *25*, 1521−1527. (b) Kobayashi, H. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1970−1973. (c) Buu-Hoi, N. P.; Saint-Ruf, G. *C. R. Acad. Sci. C* **1965**, *260*, 593−596. (d) Ramana, M. M. V.; Potnis, P. V. *J. Chem. Res., Synop.* **1996**, *4*, 175; *J. Chem. Res., Miniprint* **1996**, 0979−0994. (e) Turner, R. B.; Nettleton, D. E., Jr.; Ferebee, R. *J. Am. Chem. Soc.* **1956**, *78*, 5923−5927. (f) Katritzky, A. R.; Zhang, G. F.; Xie, L. H. *J. Org. Chem.* **1997**, *62*, 721−725. (g) Koo, S. H.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1995**, *117*, 3389−3404.

(8) Ziegler, F. E.; Chliwner, I.; Fowler, K. W.; Kanfer, S. J.; Kuo, S. J.; Sinha, N. D. *J. Am. Chem. Soc.* **1980**, *102*, 790−798.

10.1021/jo982522r CCC: $18.00
Published on Web 04/27/1999

pounds depicted in the eq 1. The yield of **2a** was increased from 44% to 60% by changing the metalation time, namely the lithiation of **1a** with *n*-BuLi (50 min reaction at −78 °C[10b] vs 20 min previously) and the subsequent transmetalation with CuI. In the same manner, three new compounds (**2b**−**2d**) were also prepared. The ^{1}H NMR spectra of these compounds showed the expected diastereotopy of the dioxomethylene protons due to the restricted rotation around the congested aryl−aryl bond. Moreover the compounds all display a W-coupling between the formyl protons and the H *meta* to it.



(1)

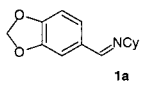
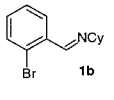
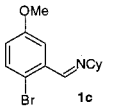
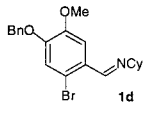
1a, R_{ij} = 3,4-OCH_2O-, Z = H
1b, R_{ij} = H, Z = Br
1c, R_{ij} = 5-OMe, Z = Br
1d, R_{ij} = 4-BnO, 5-MeO, Z = Br
1e, R_{ij} = 3,4-OCH_2O-, Z = I

2a, R_{ij} = 4',5'-OCH_2O-
2b, R_{ij} = H
2c, R_{ij} = 3'-OMe
2d, R_{ij} = 4'-BnO, 3'-MeO

The bisbenzaldehydes **2a**−**2d** obtained above were subsequently submitted to a McMurry condensation.[11] For this purpose we chose $TiCl_3$·$DME_{3/2}$/Zn(Cu)[12a] which led to the expected phenanthrenes, **3a**−**3c**, in 45−57% yields (see Table 1). These somehow moderate yields of the cyclization reaction of **2a**−**2d** could be due either to traces of water or oxygen in the reaction medium or to an unexpected sensitivity of the substrates or of the intermediates (see below) to the presence of acidic $TiCl_3$ that was not entirely reduced during the condensation reaction according to the Fürstner instant method.[12b]

However, this cyclization procedure could not be applied to the cyclization of **2d** as it led to a mixture of untractable products most probably due to side reactions induced by the O-debenzylation reaction. This result was a priori surprising since it was shown in several instances that intramolecular McMurry couplings could be achieved in the presence of benzyl-protected alcohols.[13a,b] However, debenzylation reactions were observed recently when performing the McMurry reaction in the presence of $TiCl_3$ together with reducing agents such as Li, Mg, or Zn.[14]

Table 1[a]

Substrate coupled to 2-iodopiperonalcyclohexylimine, **1e**	Isolated yields of bisbenzaldehyde	Isolated yields of phenanthrene
 **1a**	**2a** (58%)	**3a** (45%)[b]
 **1b**	**2b** (64%)	**3b** (57%)[c]
 **1c**	**2c** (70%)	**3c** (45%)[c]
 **1d**	**2d** (44%)	(d)

(a) Cy = cyclohexyl, Bn = benzyl. (b) Classical McMurry conditions, 20 hrs reflux. (c) Fürstner "instant method", 40 hrs reflux. (d) mixture of products, see text.

Compounds **3a**−**3c** have already been reported in the literature [15a−e] but they were insufficiently characterized. We provide here full spectroscopic data (^{1}H NMR, ^{13}C NMR) for all the phenanthrenes prepared.

The mechanism of the McMurry reaction is still not well understood, but it is generally accepted[13a] that it proceeds through a pinacol intermediate which undergoes deoxygenation to the corresponding olefin. In many cases the pinacol can be isolated.

We could never observed such intermediates, but we were faced with an unexpected result for the intramolecular cyclization of the nonsymmetrical **2b**. In this single case, performing the reaction for 19 h or less led to the isolation of two additional products together with the expected 3,4-(methylenedioxy)phenanthrene **3b** (eq 2). The characterization of these two side products **4b** and **5b** was difficult as they were rather unstable and difficult to handle, especially **5b**; nevertheless they were identified through their NMR and mass spectra as the bisphenanthrenol **4b** and the 9- or 10-phenanthrenol **5b**.[16] Notable features in the NMR spectra of **3b**, **4b**, and **5b** were the following: for **3b**, H_9 and H_{10} were identified as doublets (7.64 and 7.55 ppm) with a large coupling constant of 9.0 Hz. In **5b** the substitution of the double bond by an OH group induced the neighboring enol proton to be shifted to higher field (s, 6.96 ppm)[16a] while a broad singlet (5.12 ppm) is attributed to the OH proton.[16b] In the bisphenanthrenol derivative **4b** a singlet

(9) The initial Ullmann reaction was performed in the presence of copper metal around 200 °C for several hours. Ullmann, F.; Bielecki, J. *Chem. Ber.* **1901**, *34*, 2174−2185.

(10) (a) Ziegler, F. E.; Fowler, K. W.; Rodgers, W. B.; Wester, R. T. *Org. Synth.* **1987**, *65*, 108−118. (b) Ziegler, F. E.; Fowler, K. W. *J. Org. Chem.* **1976**, *41*, 1564−1566.

(11) To our knowledge the McMurry condensation as a step in the formation of the phenanthrene nucleus was limited to the synthesis of the stilbene which was then cyclized by means of a photochemical coupling: Merz, A.; Karl, A.; Futterer, T.; Stacherdinger, N.; Schneider, O.; Lex, J.; Luboch, E.; Biernat, J. F. *Liebigs Ann. Chem.* **1994**, *12*, 1199−1209. See also: Ben, I.; Castedo, L.; Saa, J. M.; Seijas, J. A.; Suau, R.; Tojo, G. *J. Org. Chem.* **1985**, *50*, 2236−2240. Experiments using a LVT strategy to form compounds related to phenanthrenes may be found in the two following papers: (a) Kadam, S. M.; Nayak, S. K.; Banerji, A. *Synth. Commun.* **1995**, *25*, 135−142. (b) Yamamoto, K.; Harada, T.; Okamoto, Y.; Chikamatsu, H.; Nakazaki, M.; Kai, Y.; Nakao, T.; Tanaka, M.; Harada, S.; Kasai, N. *J. Am. Chem. Soc.* **1988**, *110*, 3578−3584.

(12) (a) McMurry, J. E.; Lectka, T.; Rico, J. G. *J. Org. Chem.* **1989**, *54*, 3748−3749. (b) Fürstner, A.; Hupperts, A.; Ptock, A.; Janssen, E. *J. Org. Chem.* **1994**, *59*, 5215−5229.

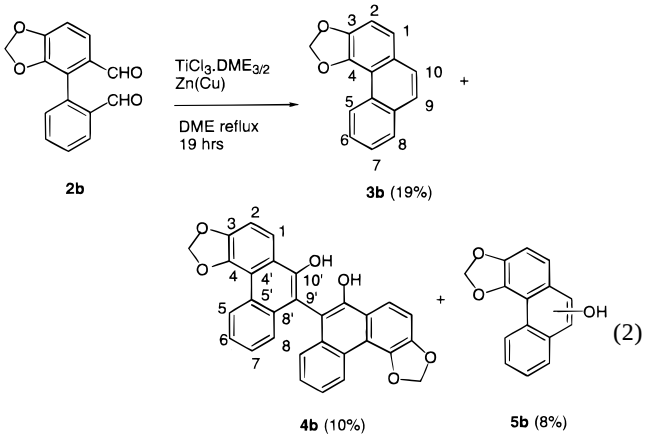
(13) (a) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513−1524 and references cited. (b) Nicolaou, K. C.; Yang, Z.; Liu, J.-J.; Nantermet, P. G.; Claiborne, C. F.; Renaud, J.; Guy, R. K.; Shibayama, K. *J. Am. Chem. Soc.* **1995**, *117*, 645−652.

(14) Talukdar, S.; Nayak, S. K.; Banerji, A. *J. Org. Chem.* **1998**, *63*, 4925−4929 and references cited.

(15) (a) Barger, G.; Weitnauer, G. *Helv. Chim. Acta* **1939**, *22*, 1036−1047. (b) Konovalova, R. A.; Yunussov, S.; Orekhov, A. *Bull. Soc. Chim. Fr.* **1940**, *7*, 70−77; *Chemical Abstracts* **1940**, *34*, 4072. (c) Shirai, H.; Oda, N. *Yakugaku Zasshi* **1959**, *79*, 241−244; *Chemical Abstracts* **1959**, *53*, 13123. (d) Shirai, H.; Oda, N. *Chem. Pharm. Bull.* **1960**, *8*, 727−731. (e) Dallacker, F.; Sommer, M.-T. *Chem.-Ztg.* **1984**, *108*, 329−331.

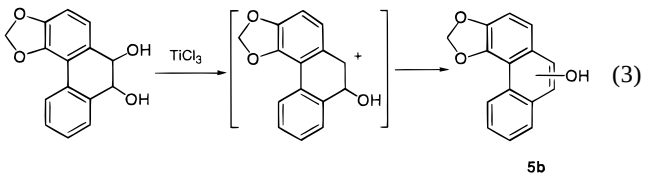
(16) (a) Nashed, N., T.; Bax, A.; Loncharich, R., J.; Sayer, J., M.; Jerina, D., M. *J. Am. Chem. Soc.* **1993**, *115*, 1711−1722. (b) Due to its unstability in solution, we could not run a ^{13}C NMR spectrum of **5b**, and thus the position of the hydroxyl substituent could not be ascertained.

due to the hydroxyl groups is found downfield at 5.42 ppm in $CDCl_3$. Noteworthy in C_6D_6 the methylene protons (5.51 and 5.48 ppm) of the dioxomethylene substituent were found to be diastereotopic due to hindered rotation around the central bond.[17] A complete assignment of the ^{13}C NMR spectrum of **4b** has been carried out via $^{13}C-^{1}H$ shift-correlated 2D NMR and $^{13}C-^{1}H$ multiple bond correlation.



Such a result would appear to be unprecedented in the literature dealing with LVT condensations, but it does not necessarily distinguish this phenanthrene synthesis from a standard McMurry reaction. Indeed, a recent investigation[18] of the mechanism, when $TiCl_3 \cdot DME_{3/2}$/Zn(Cu) was used in the condensation, has shown, inter alia, that the reflux time exerted an influence on the amount of olefin formed in the deoxygenation step. We reached the same conclusion noting that longer reflux times (ca. 40 h) for the condensation of **2b** led to increased yield of **3b**. In this latter case no **5b** could be detected whereas the amount of **4b** remained unchanged. The formation of this side product did not adversely affect our strategy as this compound can be separated from **3b**.

Despite the differences noted above, we felt that the reaction pathway of our reaction could follow the mechanism proposed by Bogdanovic and Bolte.[18] A rational explanation for the formation of **5b** would imply the reaction of a pinacol intermediate with the acidic $TiCl_3$ present as shown in the eq 3, the formation of **4b** resulting from the oxidation of **5b**.[19]



The process described in this paper, grouping Ullmann and McMurry reactions, consists of an original and unprecedented route to oxygenated phenanthrenes. Furthermore, it is likely to be amenable to many different substituted phenanthrenes starting from cheap commercially and readily available chemicals. Alternatively, the use of aromatic substrates in the McMurry condensation allows a new insight in the application and the knowledge of the reaction progress.

Experimental Section

General. All reactions were performed in a dry N_2 atmosphere using the Schlenk tube technique. Solutions were transferred by means of oven-dried syringes or cannula through rubber septa. Piperonal, vanillin, 2-bromobenzaldehyde, and 3-methoxybenzaldehyde are commercial reagents and were used without further purifications. 2-Iodopiperonal cyclohexylimine was obtained from piperonal cyclohexylimine according to a known procedure[10b] as were the other imines in this study. 6-Bromovanillin was prepared from *O*-acetylvanillin[20a] by bromination in acetic acid[20b] (HOAc). $TiCl_3 \cdot DME_{3/2}$ and Zn(Cu) were prepared according to the literature.[12a]

Anhydrous diethyl ether (Et_2O), tetrahydrofuran (THF), and dimethoxyethane (DME) were obtained from distillation on sodium/benzophenone. Anhydrous alcohol (EtOH) was obtained from distillation on sodium ethoxide. ^1H NMR and ^{13}C NMR experiments were performed at 300 and 75 MHz, respectively, except for those of **4b** which were run at 500 MHz (^1H nucleus) and 125 MHz (^{13}C nucleus) and for those of **5b** whose ^1H NMR spectrum was performed at 200 MHz (^1H nucleus). The chemical shifts, δ, are given in ppm related to TMS, and spectra are measured in $CDCl_3$. The carbons were identified through a Dept 135 experience. Microanalysis and mass spectra were performed by the Service Commun de Microanalise and the Laboratoire de Spectrométrie de Masse de Strasbourg. Spectroscopic data for **1a**,[10b] **2a**,[8] and 2-iodopiperonal cyclohexylimine[10b] are in agreement with those of the literature.

2-Bromo-5-methoxybenzaldehyde.[4e] To a suspension of 3-methoxybenzaldehyde (3.2 g, 23.4 mmol) in glacial HOAc (80 mL) was slowly added a solution of Br_2 (27.2 mmol, 1.4 mL) in HOAc (10 mL), and the reaction mixture was stirred at room temperature for 36 h. Upon addition of water (50 mL) a white suspension was formed, which was filtered and dried under vacuum. This white powder was then purified by sublimation (60 °C, 0.5 mmHg), leaving pearly crystals (3.9 g, 78%). ^1H NMR (200 MHz): 10.32 (s, 1H), 7.53 (d, $J = 8.8$ Hz, 1H), 7.42 (d, $J = 3.2$ Hz, 1H), 7.04 (dd, $J = 8.8, 3.2$ Hz, 1H), 3.85 (s, 3H).

4-Benzyloxy-5-methoxy-2-bromobenzaldehyde.[21] To a solution of 4-hydroxy-5-methoxy-2-bromobenzaldehyde (4.0 g, 17.3 mmol) in anhydrous EtOH (25 mL) were added benzyl chloride (2.6 g, 21 mmol) and K_2CO_3 (1.4 g, 10.4 mmol). The resulting suspension was refluxed for 18 h, cooled to room temperature, diluted with water, and extracted with ethyl acetate. The bright yellow organic layer was washed with brine, dried on $MgSO_4$, and filtered, and the solvent was removed in a vacuum, yielding yellow crystals (4.4 g, 79%) which were transformed into the corresponding imine without further purification. ^1H NMR: 10.16 (s, 1H), 7.44 (s, 1H), 7.44−7.33 (m, 5H), 7.09 (s, 1H), 5.18 (s, 2H), 3.89 (s, 3H).

2-Bromobenzaldehyde cyclohexylimine (1b): 89% in white crystals (*n*-hexane). ^1H NMR: 8.65 (s, 1H), 8.00 (dd, $J = 7.7, 1.9$ Hz, 1H), 7.54 (dd, $J = 7.9, 1.3$ Hz, 1H), 7.31 (dd, $J = 7.5, 7.4$ Hz, 1H), 7.22 (ddd, $J = 7.6, 7.6, 1.9$ Hz, 1H), 3.33−3.24 (m, 1H), 1.87−1.12 (m, 10H).

2-Bromo-5-methoxybenzaldehyde cyclohexylimine (1c): 76% off-white crystals (methanol). ^1H NMR (200 MHz): 8.61 (s, 1H), 7.55 (d, $J = 3.1$ Hz, 1H), 7.42 (d, $J = 8.8$ Hz, 1H), 6.83 (dd, $J = 8.8, 3.3$ Hz, 1H), 3.83 (s, 3H), 3.34−3.24 (m, 1H), 1.87−1.22 (m, 10H).

4-Benzyloxy-5-methoxy-2-bromobenzaldehyde cyclohexylimine (1d): quantitative yield of white crystals (hot CH_2Cl_2).^1H NMR: 8.54 (s, 1H), 7.57 (s, 1H), 7.45−7.32 (m, 5H), 7.04 (s, 1H), 5.14 (s, 2H), 3.93 (s, 3H), 3.30−3.21 (m, 1H), 1.87−1.20 (m, 10H).

(17) Pfeffer, M.; Sutter, J. P.; Rotteveel, M.; De Cian, A.; Fischer, J. *Tetrahedron* **1992**, *48*, 2427−2432.

(18) Bogdanovic, B.; Bolte, A. *J. Organomet. Chem.* **1995**, *502*, 109−121.

(19) We thank one of the reviewers for this suggestion.

(20) (a) Illi, V. O. *Tetrahedron lett.* **1979**, *26*, 2431−2432. (b) Raiford, L. C.; Stoesser, W. C. *J. Am. Chem. Soc.* **1927**, *49*, 1077−1080.

(21) Graf, E.; Hosseini, M. W.; Ruppert, R. *Tetrahedron lett.* **1994**, *35*, 7779−7782.

4,5:4′,5′-Bis(methylenedioxy)-6,6′-biphenyl-1,1′-dicarboxaldehyde (2a). This compound was obtained according to the literature,[10a] with the following improvements: the piperonal **1a** was reacted with *n*-BuLi during 50 min, leading to quantitative metalation. Subsequently, the transmetalation sequence to the copper complex was extended to 45 min, also resulting in a better yield for the bisbenzaldehyde **2a**: 58% of ivory crystals (hot CH_2Cl_2). ^{1}H NMR: 9.75 (s, 2H), 7.64 (d, 2H), 7.01 (d, 2H), 6.06 (d, 2H), 6.04 (d, 2H). ^{13}C NMR: 189.3 (CHO), 152.0, 146.5, 128.8, 114.8 (quaternary C), 127.1, 108.7 (CH), 102.3 (CH_2).

4,5-(Methylenedioxy)-6,6′-biphenyl-1,1′-dicarboxaldehyde (2b). To a solution of **1b** (1.0 g, 3.6 mmol) in dry THF (100 mL) at − 78 °C was added *n*-BuLi (2.5 mL of 1.6 M in hexanes, 1.1 equiv), forming a deep orange solution. After the mixture was stirred for 15−20 min, CuI·$P(OEt)_3$ (2 g, 5.4 mmol, 1.5 equiv) was added in one portion and the solution was stirred for 30−45 min. The resulting deep red solution was treated with **1e** (1.3 g, 3.6 mmol). The bright orange suspension was allowed to warm slowly to room temperature over a 2−3 h period of time and stirred for an additional 15 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and 15% aqueous HOAc (60 mL) and stirred vigorously for 15 h. The yellow solution was transferred to a 1-L separatory funnel, and the layers were separated. The organic layer was dried ($MgSO_4$), filtered, and washed with 10% aqueous HCl (3 × 100 mL) and a saturated aqueous Na_2CO_3 solution (4 × 50 mL) until the disappearance of the intense blue color of the solution. The organic layer was finally washed with brine (2 × 50 mL) and dried over $MgSO_4$, filtered, and concentrated to provide after crystallization in CH_2Cl_2 0.58 g (64%) of **2b** as pearly crystals. ^{1}H NMR (^{1}H−^{1}H COSY): 9.93 (d, $^5J_{CHO(1')-H3'} = 0.6$ Hz, CHO(1′)), 9.70 (d, $^5J_{CHO(1)-H3} = 0.6$ Hz, CHO(1)), 8.07 (ddd, $^3J_{H2'-H3'} = 7.7$ Hz, $^4J_{H2'-H4'} = 1.6$ Hz, $^5J_{H2'-H5'} = 0.5$ Hz, $H_{2'}$), 7.69 (td, $^3J_{H4'-H3',5'} = 7.4$ Hz, $^4J_{H4'-H2'} = 1.3$ Hz, $H_{4'}$), 7.67 (d, $^3J_{H2-H3} = 8.2$ Hz, H_2), 7.60 (tdd, $^3J_{H3'-H4',2'} = 7.6$ Hz, $^4J_{H3'-H5'} = 1.4$ Hz, $^5J_{H3'-CHO(1')} = 0.6$ Hz, $H_{3'}$), 7.36 (ddd, $^3J_{H5'-H4'} = 7.5$ Hz, $^4J_{H5'-H3'} = 1.4$ Hz, $^5J_{H5'-H2'} = 0.5$ Hz, $H_{5'}$), 7.01 (dd, $^3J_{H3-H2} = 8.0$ Hz, $^5J_{H3-CHO(1)} = 0.6$ Hz, H_3), 6.04 (d, $^2J = 1.1$ Hz, 1H, OCH_2O), 6.02 (d, $^2J = 1.2$ Hz, 1H, OCH_2O).^{13}C NMR: 190.9, 189.2 (CHO), 151.7, 146.4, 134.7, 134.2, 129.2, 121.2 (quaternary C), 133.6, 132.0, 129.0, 128.6, 126.7, 108.5 (CH), 102.4 (CH_2). Anal. Calcd for $C_{15}H_{10}O_4$: C, 70.86; H, 3.96. Found: C, 71.43; H, 4.08.

3′-Methoxy-4,5-(methylenedioxy)-6,6′-biphenyl-1,1′-dicarboxaldehyde (2c): 70% of white crystals (CH_2Cl_2 twice). ^{1}H NMR: 9.86 (s, 1H), 9.70 (d, $J = 0.5$ Hz, 1H), 7.66 (d, $J = 8.2$ Hz, 1H), 7.55 (d, $J = 2.6$ Hz, 1H), 7.27 (dd, $J = 8.5$, 0.5 Hz, 1H), 7.22 (dd, $J = 8.5$, 2.6 Hz, 1H), 6.99 (d, $J = 8.0$ Hz, 1H), 6.04 (d, $J = 1.0$ Hz, 1H), 6.02 (d, $J = 1.1$ Hz, 1H), 3.91 (s, 3H). ^{13}C NMR: 190.6, 189.3 (CHO), 160.1, 151.6, 146.5, 135.3, 129.6, 127.1, 121.3 (quaternary C), 133.2, 123.7, 120.9, 111.4 108.5 (CH), 102.2 (CH_2), 55.6 (CH_3). Anal. Calcd for $C_{16}H_{12}O_5$: C, 67.60; H, 4.26. Found: C, 67.02; H, 4.36.

4′-Benzyloxy-3′-methoxy-4,5-(methylenedioxy)-6,6′-biphenyl-1,1′-dicarboxaldehyde (2d): 44% of light yellow crystals (CH_2Cl_2). ^{1}H NMR: 9.71 (s, 1H), 9.59 (d, $J = 0.5$ Hz, 1H), 7.63 (d, $J = 8.2$ Hz, 1H), 7.57 (s, 1H), 7.40−7.25 (m, 5H), 6.96 (dd, $J = 8.2$, 0.5 Hz, 1H), 6.82 (s, 1H), 6.00 (d, $J = 1.0$ Hz, 1H), 5.97 (d, $J = 1.3$ Hz, 1H), 5.17 (s, 2H), 3.96 (s, 3H). ^{13}C NMR: 189.5, 189.0 (CHO), 152.6, 151.6, 150.0, 146.5, 135.5, 129.6, 129.2, 127.9, 121.1 (quaternary C), 128.6, 128.6, 128.2, 127.3, 127.3, 125.9, 115.6, 109.5, 108.6 (CH), 102.3, 70.9 (CH_2); 56.0 (CH_3). Anal. Calcd for $C_{23}H_{18}O_6$: C, 70.76; H, 4.65. Found: C, 70.21; H, 5.31.

McMurry Condensation. The classical McMurry process[12a] was employed for the preparation of **3a** whereas in the other cases the so-called "instant method" described by Fürstner and co-workers[12b] was preferred. These two routes only differed in the experimental conditions since in the latter case no reflux was required to activate the LVT reagent prior to the addition of the substrate. In our case the yield of phenanthrene was barely different in the two methodologies depending only on the reflux time. An alternative catalytic path[22] was tried that only led to an untractable mixture likely to comprise the phenanthrene.

3,4:5,6-Bis(methylenedioxy)phenanthrene (3a). A flame-dried two necked 500-mL round-bottomed flask was charged with $TiCl_3$·$DME_{3/2}$ (6.6 g, 23 mmol) and Zn(Cu) (5.2 g, 80 mmol) under a nitrogen atmosphere, and dry DME (250 mL) was added. The slurry was heated to reflux for ca. 5 h under a weak flow of N_2 and appeared as a deep purple mixture. A solution of **2a** (0.833 g, 2.8 mmol) in DME (50 mL) was then added over 3 h by means of a syringe pump. The reaction mixture turned black. After 20 h of reflux, the residual solids were removed by filtering twice over a pad of Celite and the solvent was partialy removed under reduced pressure. The pad was washed with Et_2O, giving rise to a yellow-brown solution. The combined organic washes were subjected to silica chromatography (acetone:*n*-hexane, 40:60), affording 0.336 g of beige crystals (45%) which were recrystallized from boiling MeOH. ^{1}H NMR: 7.39 (s, 2H), 7.35 (d, $J = 8.2$ Hz, 2H), 7.19 (d, $J = 8.2$ Hz, 2H), 6.16 (s, 4H). ^{13}C NMR: 145.8,143.0, 128.9, 112.5 (quaternary C), 125.1, 122.1, 109.4 (CH), 100.5 (CH_2). Anal. Calcd for $C_{16}H_{10}O_4$: C, 72.18; H, 3.79. Found: C, 72.22; H, 4.13. MS (EI) *m/z*: calcd 266.3, found 266.1 (M^+).

3,4-(Methylenedioxy)phenanthrene (3b). In a dry Schlenck tube equipped with a magnetic stirrer, **2b** (0.5 g, 1.97 mmol), $TiCl_3$·$DME_{3/2}$ (4.67 g, 0.016 mol, 8 equiv), and Zn(Cu) (4.0 g, 0.060 mol, 30 equiv) in dry DME (30 mL) were heated to reflux for 40 h under a weak flow of nitrogen. The black slurry was then cooled to room temperature and carefully filtered over a pad of Celite to leave a light yellow solution. The pad was washed twice with CH_2Cl_2. The solvent was removed under reduced pressure, leaving a light brown solid which in chloroform separated into a purple gel and a light yellow solution. Both the fractions were analyzed by TLC (CH_2Cl_2:*n*-hexane, 50:50) and revealed the presence of **3b** ($R_f = 0.60$) with a more polar compound ($R_f = 0.10$). Flash chromatographic separation (acetone:*n*-hexane, 2:98; acetone was the only solvent found to solubilize the purple residue) afforded 0.3 g of a very thick colorless oil from which the desired phenanthrene was crystallized in hot EtOH, affording **3b** as white crystals (0.25 g, 57%). A bright yellow highly polar fraction was then eluted with 100% acetone and was found to be the side product **4b** (yellow powder, 0.05 g (10%), turns green in solution). Under the above conditions, no trace of **5b** was found. However, starting with the same amount of reagents but after only 19 h reflux, elution of the crude mixture (Et_2O:*n*-hexane, 30:70) gave rise to **3b** (19%, $R_f = 0.77$), **4b** (10%, $R_f = 0.38$), and **5b** (8%, $R_f = 0.21$).

3b. ^{1}H NMR: 9.06 (dd, $J = 8.5$, 2.0 Hz, 1H), 7.86−7.82 (m, 1H), 7.64 (d, $J = 9.0$ Hz, 1H), 7.63−7.58 (m, 2H), 7.55 (d, $J = 9.0$ Hz, 1H), 7.44 (d, $J = 8.5$ Hz, 1H), 7.22 (d, $J = 8.2$ Hz, 1H), 6.26 (s, 2H). ^{13}C NMR: 145.4, 143.3, 132.3, 128.5, 128.2, 116.6 (quaternary C), 127.8, 127.2, 127.0, 126.7, 126.2, 124.9, 122.0, 109.0 (CH), 101.2 (CH_2). Anal. Calcd for $C_{15}H_{10}O_2$: C, 81.07; H, 4.54. Found: C, 81.14; H, 4.96.

Bis(3,4-(methylenedioxy)-9(10)-phenanthrenol) (4b). ^{1}H NMR: 9.20 (dd, $J = 8.0$, 1.1 Hz, 1H), 8.41 (dd, $J = 7.8$, 1.4 Hz, 1H), 7.81−7.69 (m, 2H), 6.97 (d, $J = 8.5$ Hz, 1H), 6.83 (d, $J = 8.5$ Hz, 1H), 6.28 (s, 2H), 5.41 (broad s, OH). ^{13}C NMR: 147.8 (C9), 144.5 (C3), 144.0 (C4), 129.9 (C5′), 128.0 (C5), 127.4 (C10′), 127.2 (C6), 127.0 (C7), 125.2 (C8′), 122.9 (C8), 118.4 (C1 or C2), 113.8 (C4′), 109.8 (C1 or C2), 107.5 (C10), 101.4 (CH_2). MS (EI) *m/z*: calcd for $C_{30}H_{18}O_6$ 474.5, found 474.3 (M^+).

3,4-(Methylenedioxy)-9-(10)phenanthrenol (5b). ^{1}H NMR: 9.09−9.03 (m, 1H), 8.28−8.23 (m, 1H), 7.70−7.61 (m, 2H), 7.24 (d, $J = 8.3$ Hz, 1H), 7.16 (d, $J = 8.3$ Hz, 1H), 6.96 (s, 1H), 6.24 (s, 2H), 5.12 (broad s, OH). MS (EI) *m/z:* calcd for $C_{15}H_{10}O_3$ 238.2, found 238.0 (M^+).

2-Methoxy-5,6-(methylenedioxy)phenanthrene (3c). In a dry Schlenck tube equipped with a magnetic stirrer, **2c** (0.52 g, 0.0018 mol), $TiCl_3$·$DME_{3/2}$ (4.70 g, 0.016 mol, 8.9 equiv), and

(22) Fürstner, A.; Hupperts, A. *J. Am. Chem. Soc.* **1995**, *117*, 4468−4475.

Zn(Cu) (5.1 g, 0.076 mol, 42 equiv) in dry DME (30 mL) were heated to reflux for 40 h under a weak flow of nitrogen. The black slurry was cooled to room temperature and carefully filtered over a pad of Celite to leave a light yellow solution. The pad was washed twice with CH_2Cl_2. The solvent was removed under reduced pressure, spontaneously yielding an off-white solid (0.25 g, 45%) which was further purified by preparative TLC on silica with Et_2O:*n*-hexane, 70:30 (R_f = 0.68). ^{1}H NMR: 8.95 (d, J = 9.9 Hz, 1H), 7.62 (d, J = 8.9 Hz, 1H), 7.48 (d, J = 8.9 Hz, 1H), 7.42 (d, J = 8.2 Hz, 1H), 7.26−7.22 (m, 2H), 7.16 (d, J = 8.4 Hz, 1H), 6.25 (s, 2H), 3.96 (s, 3H). ^{13}C NMR: 158.1, 145.3, 142.5 (C−O), 133.8, 128.6, 122.3, 116.6 (quaternary C), 128.7, 127.6, 124.5, 122.1, 116.0, 108.4, 108.2 (CH), 101.1 (CH_2), 55.2 (CH_3). Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 75.56; H, 5.12.

Acknowledgment. We thank Dr. Roland Graff for his help in performing and elucidating the 2D NMR experiments.

Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra of compounds **2a**−**d**, **3a**−**c**, **4b**, and **5b**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO982522R