A Novel Nickel(0)-Mediated One-Pot Cascade Reaction to *cis*-9,10-Dihydroxy-9,10-dihydrophenanthrenes and 9-Phenanthrones

Helge A. Reisch, Volker Enkelmann, and Ullrich Scherf*

Max-Planck-Institut für Polymerforschung, Ackermannweg 10, D-55128 Mainz, Germany

Received August 26, 1998

Introduction

Ni(0)-mediated aryl−aryl homocouplings of haloaryl compounds represent a highly potent, very efficient method for the synthesis of biaryls and oligo- or polyaryls. The method is applicable in the presence of a broad variety of additional functional groups (e.g., ether, aldehyde, keto, amino, and nitro substituents) which remain unreacted after the aryl−aryl coupling.[1] The original variant for this homocoupling of arylhalides, described by Semmelhack et al., is based on stoichiometric amounts of preformed Ni(0) reagents.[2] This procedure was extended to Ni(0) reagents generated in situ[3] and also adapted to catalytic amounts of Ni(0) reagents in the presence of an additional reducing agent.[4] Yamamoto et al. described the application of this efficient coupling reaction on the synthesis of polyaryls starting from bihalo monomers, by means of 1.2 equiv of the $Ni(COD)_2$ reagent per aryl−aryl bond formed.[5]

Results and Discussion

In this note, we describe homocoupling experiments of 2-carbonyl-substituted bromobenzenes **1** with an excess (1.2−2.2 equiv per aryl−aryl bond formed) of the $Ni(COD)_2$ reagent. For this variant of the coupling reaction, the 2,2′-keto- or aldehyde-substituted biphenyls **2** generated in the initial aryl−aryl coupling step do not represent the final reaction products. The aryl−aryl coupled intermediates undergo a subsequent intramolecular pinacol-type cyclization which leads stereoselectively to *cis*-9,10-dihydroxy-9,10-dihydrophenanthrene derivatives **3**. Both reaction steps of this one-pot reaction cascade are effected by the $Ni(COD)_2$ reagent. The novel reaction sequence provides the cyclic products **3** in excellent yields of up to 98%, representing, therefore, a very simple one-pot method for the generation of *cis*-9,10-dihydroxy-9,10-dihydrophenanthrenes **3**. If the substituents R at the 9- and 10-positions of the phenanthrene skeleton are characterized by an additional tendency to undergo acid-catalyzed cationic rearrangements, the resulting pinacols **3** can be completely converted into the corresponding pinacolones **4** during an acidic workup procedure. Thus, the phenanthrone derivatives **4a** and **4b** are available in high yields starting from the corresponding 2-bromobenzophenones **1a** and **1b** in a one-pot reaction.

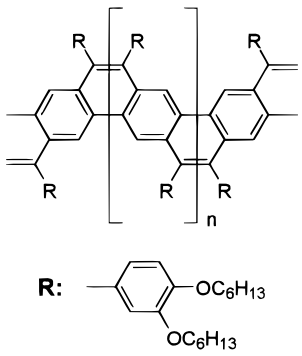


Figure 1. Poly(*p*-phenacene).

Our experiments were part of a project dealing with the synthesis of low-molecular-weight model compounds of poly(*p*-phenacene) ladder polymers[6] (Figure 1), fully aromatic ribbon polymers which were synthesized in 1993 by Chmil and Scherf. The ladder polymers were generated in a two-step reaction sequence involving an aryl−aryl coupling according to Yamamoto[5] followed by a polymer-analogous olefination of the keto functions.

First, we have tried to synthesize the diketo model compound **2a** under the conditions of the polymer reaction, using a slight excess of the transition-metal reagent $Ni(COD)_2$ (1.2 equiv per aryl−aryl bond), together with 2,2′-bipyridine and 1,5-cyclooctadiene as coreagents. For this, a solution of the bromo compound **1a** dissolved in dry DMF was added to the purple solution of the nickel complex in dry DMF at 60 °C. After acidic workup, the expected aryl−aryl coupled diketone **2a** was obtained in 78% yield. However, we could isolate a byproduct in about 20% yield, which was unambiguously identified as the pinacolone **4a**. This unexpected result implies that the initial aryl−aryl coupling product can undergo a further intramolecular cyclization to the pinacol **3a** (Scheme 1) under the reaction conditions of the Ni(0)-mediated aryl−aryl coupling. The pinacolone **4a** was then generated during the acidic workup with 2 N HCl. To explore the synthetic scope of this cascade reaction in more detail, we have reacted the 2-bromobenzophenone derivatives **1a**,**b** and 2-bromobenzaldehyde (**1c**) with varying amounts of $Ni(COD)_2$.

The results of this reaction series are listed in Table 1. To prevent the pinacol−pinacolone rearrangement of **3** to **4**, we have applied a modified neutral, nonacidic workup procedure (for details see Experimental Section). Under these reaction conditions, the reaction mixtures were composed only of the pinacols **3** and the diketones **2** as products (entries 1−3). The product ratio **3**/**2** was in each case about 20:80 if 1.2 equiv of $Ni(COD)_2$ per aryl−aryl bond was used. When the amount of the $Ni(COD)_2$ reagent was increased to 2.2 equiv, formation of the pinacol **3** becomes the dominant reaction. Hereby, in a first variant, the bromo compounds **1a**−**c** were added in one portion to the solution of the nickel complex. The

* E-mail: scherf@mpip-mainz.mpg.de. Tel: +49-6131-379306. Fax: +49-6131-379100.

(1) Wilke, G. *The Organic Chemistry of Nickel;* Academic Press: New York, 1975; Vol. II, p 246.
(2) Semmelhack, M. F.; Helquist, P. M.; Jones, L. D. *J. Am. Chem. Soc.* **1971**, *93*, 5908.
(3) Kende, A. S.; Liebeskind, L. S.; Braitsch, D. M. *Tetrahedron Lett.* **1975**, 3375.
(4) Colon, I.; Kelsey, D. R. *J. Org. Chem.* **1986**, *51*, 2627.
(5) Yamamoto, T.; Morita, A.; Miyazaki, Y.; Maruyama, T.; Wakayama, H.; Zhou, Z.; Nakamura, Y.; Kanbara, T.; Sasaki, S.; Kubota, K. *Macromolecules* **1992**, *25*, 1214−1223.
(6) Scherf, U.; Chmil, K. *Acta Polym.* **1997**, *48*, 208.

10.1021/jo9817523 CCC: $18.00
Published on Web 12/29/1998

Scheme 1. Reaction Scheme of the Nickel(0)-Mediated Cascade Reaction

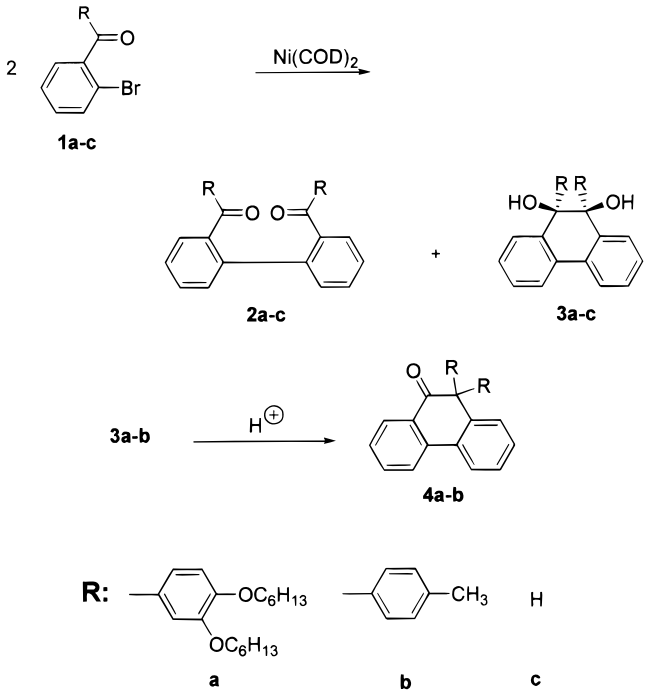


Table 1. Reaction Data of the Cascade Reaction of 1a−c to 2a−c/3a−c

entry no	R	$Ni(COD)_2$ (equiv)	total yield **2** and **3** (%)	ratio **2**:**3** (%)
1	**a**	1.2[a]	92	78:22
2	**b**	1.2[a]	96	76:24
3	**c**	1.2[a]	96	84:16
4	**a**	2.2[a]	94	9:91
5	**b**	2.2[a]	97	10:90
6	**c**	2.2[a]	99	17:83
7	**a**	2.2[b]	97	0:100
8	**b**	2.2[b]	99	0:100
9	**c**	2.2[b]	100	8:92

[a] Addition of the bromo compound in one portion. [b] Slow addition of the bromo compound over a time period of 20 min.

pinacols **3** were then obtained in rather high yields of 83−91% (entry 4−6). These yields could be further improved in a slightly varied reaction methodology in which the educts **1a**−**c** are slowly added to the solution of the Ni(0) reagent. For this special variant, the phenyl substituted products **3a,b** could be isolated in nearly quantitative yields, and the unsubstituted phenanthrene pinacol **3c** in almost 92% yield (entries 7−9). Monitoring the progress of the reaction by HPLC, we have found that the two-step reaction proceeds very fast and is almost completed after 4−5 min.

The cyclization can lead, in principle, to the *cis*- or *trans*-configured product **3**. However, the ^1H and ^{13}C spectra indicate that only one of the two possible isomers is formed. The formation of the pinacols is, therefore, highly stereoselective. Because both of the stereoisomeres of pinacol **3c** (R = H) were described in the literature, we have initially concentrated on the structural analysis of **3c**. However, the literature data for *cis*- and *trans*-**3c** are not consistent, the melting points given for *trans*-**3c** differ, for example, by more than 30 °C.[7] To overcome these shortcomings, we have crystallized **3b** and verified its structure by X-ray crystal structure analysis. As a result, we could characterize compound **3b** as the *cis*-isomer (Figure 2). This *cis*-configuration of **3b** is a clear indication that the cyclization step of **2b** to **3b** should involve a cyclic intermediate in which a Ni(0) center coordinates two carbonyl functions. To prove this mechanistic assumption, we have also reacted the preformed 2,2′-substituted biphenyls **2a**−**c** with 1.2 equiv of $Ni(COD)_2$. In this case, we could isolate the intramolecularly cyclized pinacols **3a**−**c** in nearly quantitative yields, as expected (Scheme 2).

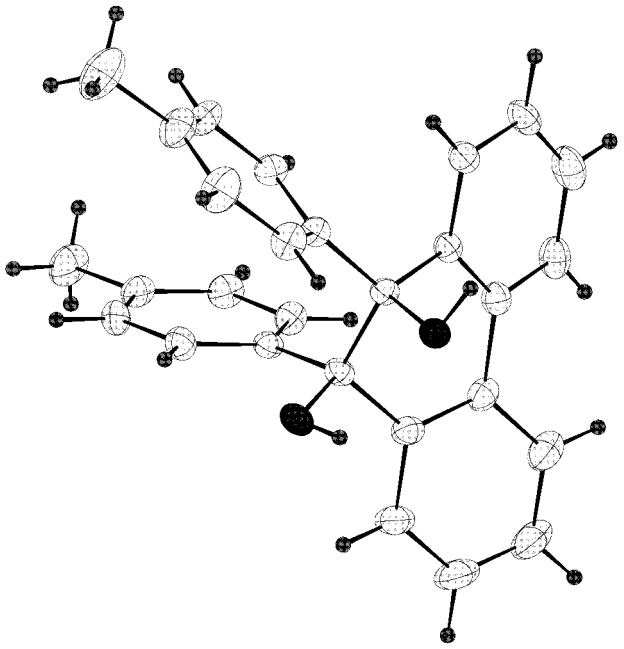
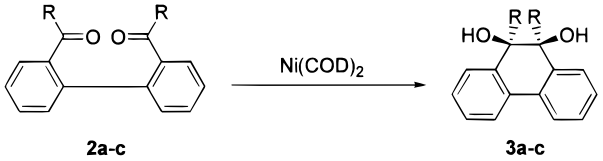


Figure 2. X-ray structure of *cis*-9,10-dihydroxy-9,10-dihydrophenanthrene (**3b**).

Scheme 2. Intramolecular Cyclization of 2a−c to the *cis*-Pinacols 3a−c



The proposed mechanism for the Ni(0)-mediated cyclization is shown in Scheme 3. On the basis of our findings, the reaction sequence starting from **1a**−**c** involves two reaction steps: (1) formation of the 2,2′-substituted biphenyl intermediates via aryl−aryl coupling and (2) intramolecular cyclization to the corresponding pinacols.

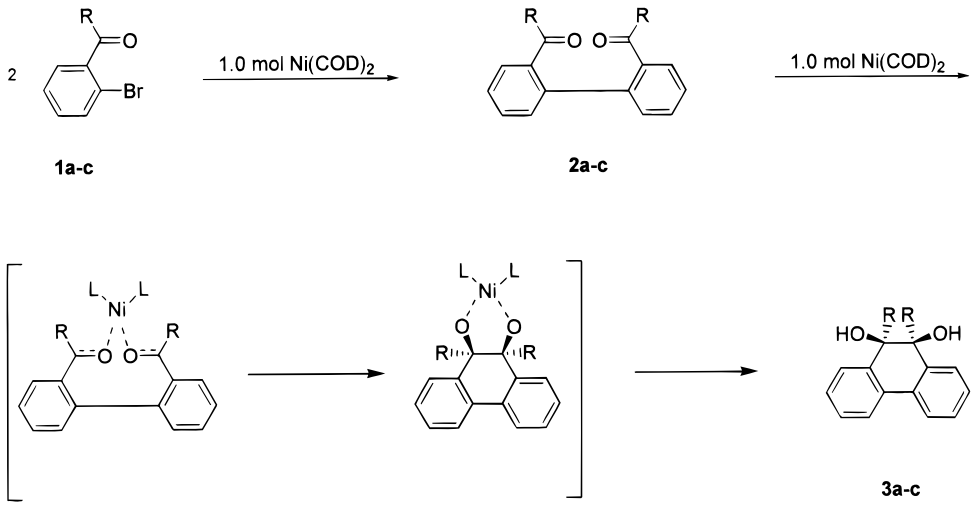
We have also investigated whether the above-described *intra*molecular Ni(0)-mediated pinacol cyclization can also proceed as an *inter*molecular process starting from aromatic ketones or benzaldehyde. Unfortunately, all attempts to couple such carbonyl compounds failed, and we always isolated the unreacted educts (Scheme 4). Therefore, the Ni(0)-mediated pinacol cyclization seems to be restricted to *intra*molecular cyclizations, e.g., that of 2,2′-substituted biaryls.

Conclusion

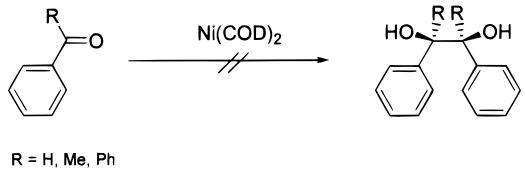
The 2-bromobenzophenones **1a,b** and 2-bromobenzaldehyde (**1c**) can be transformed to the pinacols **3a**−**c** in

(7) Platt, K. L.; Oesch, F. *Synthesis* **1982**, 459. Miura, R.; Honmaru, S.; Nakazaki, M. *Tetrahedron Lett.* **1968**, *50*, 5271.

Scheme 3. Proposed Mechanism for the Formation of the Pinacols 3 from the Biphenyl Intermediates 2



Scheme 4. Reaction of Aromatic Ketones and Benzaldehyde with $Ni(COD)_2$



a one-pot, nickel(0)-mediated cascade reaction in excellent yields. The reaction occurs stereoselectively, and only the *cis*-diol was isolated. The corresponding pinacolones **4a,b** have been obtained under acid workup conditions. The novel reaction sequence defines an efficient synthetic method for the generation of *cis*-9,10-dihydroxy-9,10-dihydrophenanthrenes and the corresponding 9-phenanthrones in a one-pot process. However, the Ni(0)-mediated pinacol cyclization as second step of the reaction sequence is restricted to *intra*molecular processes. Benzaldehyde or aromatic ketones do not yield the corresponding pinacols when reacted with $Ni(COD)_2$. Further studies are planned to carry out the novel cascade reaction with catalytic amounts of the Ni(0) complex in the presence of an additonal reducing agent (e.g., Zn).

Experimental Section

2-Bromobenzaldehyde and 2-bromobenzoyl chloride were obtained from Aldrich and were used without further purification. The melting points are not corrected.

X-ray Crystallography. Data were collected on a diffractometer with graphite monochromated Mo Kα radiation (λ = 0.71069 Å) at 210 K. The structure was solved by direct methods (SIR92) and refined by full-matrix least-squares analyses with anisotropic temperature factors for C and O. The H atoms were refined with fixed isotropic temperature factors in the riding mode. No absorption correction was applied.

2-Bromo-4′-methylbenzophenone (1b). A solution of anhydrous $AlCl_3$ (4.0 g, 30 mmol) in 50 mL of toluene at 0 °C was treated with a solution of 2-bromobenzoyl chloride (5.0 g, 28 mmol) in 20 mL of methylene chloride. The resulting mixture was stirred at 25 °C for 24 h, poured into 30 g of ice, and extracted with CH_2Cl_2. The organic phase was washed several times with diluted hydrochloric acid and H_2O. After drying over $MgSO_4$, concentration in vacuo, and recrystallization from hexane, **1b** was obtained (5.76 g, 92%). Mp: 91 °C. ^{1}H NMR (500 MHz, $C_2D_2Cl_4$): δ = 7.61 (d, ^3J = 8.0 Hz, 2H), 7.58 (dd, ^3J = 7.6 Hz, ^4J = 1.0 Hz, 1H,), 7.35 (dt, ^3J = 7.6 Hz, ^4J = 1.0 Hz, 1H), 7.29 (dt, ^3J = 7.6 Hz, ^4J = 1.8 Hz, 1H), 7.25 (dd, ^3J = 7.6 Hz, ^4J = 1.8 Hz, 1H), 7.20 (d, ^3J = 8.0 Hz, 2H), 2.35 (s, 3H, $-CH_3$). ^{13}C NMR (125 MHz, $C_2D_2Cl_4$): δ = 195.8, 145.3, 141.0, 133.8, 133.5, 131.5, 130.6, 129.7, 129.3, 127.5, 119.7, 22.2. FD-MS: m/z = 275.9. Anal. Calcd for $C_{14}H_{11}BrO$ (275.1): C, 61.11; H, 4.03; Br, 29.04. Found: C, 61.01; H, 4.03; Br, 28,73.

2-Bromo-3′,4′-dihexyloxybenzophenone (1b). The reaction of 2-bromobenzoyl chloride with 1,2-dihexyloxybenzene was performed as described for **1b**. Recrystallization from methanol gave **1a** in 82% yield. Mp: 48−49 °C. ^{1}H NMR (500 MHz, $C_2D_2Cl_4$): δ = 7.59 (dd, ^3J = 7.9 Hz, ^4J = 1.0 Hz, 1H), 7.42 (d, ^4J = 2.0 Hz, 1H), 7.36 (dt, ^3J = 7.5 Hz, ^4J = 1.0 Hz, 1H,), 7.30 (dd, ^3J = 7.8 Hz, ^4J = 1.8 Hz, 1H), 7.28 (dt, ^3J = 7.4 Hz, ^4J = 1.8 Hz, 1H), 7.13 (dd, ^3J = 8.4 Hz, ^4J = 2.0 Hz, 1H), 6.76 (d, ^3J = 8.5 Hz), 3.97 (m, 4H), 1.76 (m, 4H), 1.29 (m, 8H), 0.85 (m, 6H). ^{13}C NMR (125 MHz, $C_2D_2Cl_4$): δ = 194.8, 154.8, 149.4, 141.2, 133.4, 131.2, 129.2, 129.1, 127.5, 126.6, 119.8, 114.2, 112.1, 69.8, 69.4, 31.9, 31.8, 29.5, 29.3, 26.0, 22.9, 14.3. FD-MS: m/z = 461.4. Anal. Calcd for $C_{25}H_{33}BrO_3$ (460.2): C, 65.07; H, 7.21; Br, 17.32. Found: C, 64.95; H, 7.08; Br, 16,85.

***cis*-9,10-Dihydroxy-9,10-bis(4-methylphenyl)phenanthrene (3b) (Standard Procedure).** $Ni(COD)_2$ (1.59 g, 6.0 mmol), 1,5-cyclooctadiene (531 mg, 5.0 mmol), and bipyridine (937 mg, 6.0 mmol) were dissolved in 20 mL of dry DMF in a Schlenk tube under argon. 2-Bromo-4′-methylbenzophenone (**1b**) (1.37 g, 5.0 mmol) was added to the solution at room temperature. The reaction mixture was stirred at 60 °C for 3 h. After cooling to room temperature, the mixture was diluted with methylene chloride, filtered through a small pad of silica gel, and washed three times with a 10% aqueous solution of $FeCl_3$. The organic layer was separated and dried over $MgSO_4$. The solvent was removed in vacuo, and the crude product was purified by column chromatography on silica gel (ethyl acetate/hexane, 1/4) to yield **3b** (0.97 g, 99%).[8] Mp: 186−187 °C (decomp. ^{1}H NMR (500 MHz, $C_6D_4Cl_2$, 438 K): δ = 7.92 (d, ^3J = 7.8 Hz, 2H), 7.39 (t, ^3J = 7.8 Hz, 2H, H-3), 7.33 (d, ^3J = 7.6 Hz, 2H), 7.21 (t, ^3J = 7.6 Hz, 2H), 6.80 (d, ^3J = 8.0 Hz, 4H), 6.74 (d, ^3J = 7.9 Hz, 4H), 3.0 (s, 2H), 2.25 (s, 6H). FD-MS: m/z = 392.4. Anal. Calcd for $C_{28}H_{24}O_2$ (392.5): C, 85.86; H, 6.16. Found: C, 85.62; H, 6.03. Crystal data for **3b** (crystallized from methanol): $C_{28}H_{24}O_2$, monoclinic, space group $P2_1$; a = 10.2647(6), b = 9.7202(3), c = 10.8440(6) Å; β = 101.719(2)°, V = 1059.4 Å^3, Z = 2, D_x = 1.230, m(MoKα) = 0.707 cm^{-1}. A crystal with dimensions 0.4 × 0.25 × 0.1 mm^3 was used for the data collection. In addition, 2429 unique reflections were measured, of which 1975 were observed ($I > 3\sigma(I)$). R = 0.044, R_w = 0.042 (unit weights).

***cis*-9,10-Dihydroxy-9,10-bis(3,4-dihexyloxyphenyl)-phenanthrene (3a).** Using our standard procedure, the coupling of **1a** (1.04 g, 2.25 mmol) gave **3a** (0.85 g, 97%),[8] which

(8) The products **3a** and **3b** exhibit complex ^{13}C NMR spectra at ambient temperature, suggesting that the rotation of the aryl rings in the 9- and 10-positions of the phenanthrene skeleton is restricted. Even at 165 °C in 1,4-$C_6D_4Cl_2$, we could not obtain well-resolved ^{13}C NMR spectra.

was purifed by column chromatography (ethyl acetate/hexane, 1/10). Mp: 74−76 °C. ^{1}H NMR (500 MHz, *p*-$C_6D_4Cl_2$, 438 K): δ = 7.85 (d, ^3J = 6.3 Hz, 1H), 7.74 (d, ^3J = 6.1 Hz, 1H), 7.60 (d, ^3J = 7.3 Hz, 1H), 7.19−7.14 (m, 2H), 7.03 (m, 1H), 6.94 (m, 2H), 6.67 (s, 2H), 6.62 (d, ^3J = 7.9 Hz, 2H), 6.51 (d, ^3J = 7.9 Hz, 2H), 3.76 (m, 8H), 1.55 (m, 8H), 1.31−1.14 (m, 24H), 0.73 (m, 12H). FD-MS: *m*/*z* = 764.2. Anal. Calcd for $C_{50}H_{68}O_6$ (765.1): C, 78.49; H, 8.92. Found: C, 78.32; H, 8.86.

***cis*-9,10-Dihydroxy-9,10-dihydrophenanthrene (3c).** Using our standard procedure, 2-bromobenzaldehyde (1.50 g, 8.11 mmol) was coupled to **3c** (0.85 g, 100%), which was purifed by column chromatography (ethyl acetate/hexane, 1/10). Mp: 180−181 °C (decomp) (lit. 178−179 °C)[9]. ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 7.77 (d, ^3J = 7.7 Hz, 2H), 7.65 (d, ^3J = 7.7 Hz, 2H), 7.42−7.36 (m, 4H), 4.71 (s, 2H), 2.65 (s, 2H). ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 136.8, 132.8, 128.7, 128.6, 125.6, 124.0, 74.3. FD-MS: *m*/*z* = 212.2. Anal. Calcd for $C_{14}H_{12}O_6$ (210.2): C, 79.22; H, 5.70. Found: C, 79.10; H, 5.76.

Acidic Workup for the Preparation of the 9-Phenanthrones 4a/b. The reaction mixture, after the coupling of **1a** or **1b**, was poured into methanolic HCl, stirred for 24 h at 25 °C, and extracted twice with methylene chloride. The organic phase was washed with water and dried over $MgSO_4$. Concentration in vacuo, followed by recrystallization or column chromatography gave the 9-phenanthrones **4a** or **4b**.

10,10-Bis(3,4-dihexyloxyphenyl)-9-phenanthrone (4a). The acidic workup, followed by column chromatography (ethyl acetate/hexane, 1/10), yielded **4a** (1.0 g, 93%) as a viscous oil. ^{1}H NMR (500 MHz, $C_2D_2Cl_4$, 135 °C): δ = 7.94 (d, ^3J = 8.0 Hz, 1H), 7.89 (d, ^3J = 7.8 Hz, 1H), 7.86 (d, ^3J = 8.0 Hz, 1H), 7.53 (dd, ^3J = 8.0 Hz, ^3J = 7.6 Hz, 1H), 7.37 (dd, ^3J = 8.0 Hz, ^3J = 7.2 Hz, 1H), 7.31 (dd, ^3J = 7.8 Hz, ^3J = 7.6 Hz, 1H), 7.22 (dd, ^3J = 7.8 Hz, ^3J = 7.2 Hz, 1H), 6.84 (d, ^3J = 7.8 Hz, 1H), 6.71 (d, ^3J = 8.5 Hz, 2H), 6.55 (d, ^4J = 2.0 Hz, 2H), 6.44 (dd, ^3J = 8.5 Hz, ^4J = 2.0 Hz, 2H), 3.95 (t, ^3J = 6.5 Hz, 4H), 3.80 (t, ^3J = 6.5 Hz, 4H), 1.74 (m, 4H), 1.62 (m, 4H), 1.37−1.28 (m, 24H), 0.92−0.87 (m, 12H). ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, 135 °C): δ = 200.1, 149.6, 149.5, 142.4, 137.1, 135.3, 133.8, 132.3, 131.8, 131.2, 128.6, 128.4, 128.2, 127.9, 124.2, 123.9, 122.9, 119.3, 115.2, 70.6, 70.1, 67.8, 31.8, 29.9, 29.8, 26.0, 25.9, 22.7, 22.6, 13.9. FD-MS: *m*/*z* = 746.5. Anal. Calcd for $C_{50}H_{66}O_5$ (747.1): C, 80.39; H, 8.90. Found: C, 80.26; H, 8.62.

10,10-Bis(4-methylphenyl)-9-phenanthrone (4b). Applying the acidic workup, followed by recrystallization from methanol, we obtained **4b** (0.90 g, 96%). Mp: 208−209 °C. ^{1}H NMR (500 MHz, $C_2D_2Cl_4$): δ = 7.93 (d, ^3J = 7.9 Hz, 1H), 7.85 (d, ^3J = 7.9 Hz, 2H), 7.53 (m, 1H), 7.35 (m, 1H), 7.29 (m, 1H), 7.19 (m, 1H), 6.97 (d, ^3J = 8.2 Hz, 4H), 6.74 (d, ^3J = 8.2 Hz, 4H), 6.72 (d, 1H), 2.24 (s, 6H). ^{13}C NMR (125 MHz, $C_2D_2Cl_4$): δ = 201.0, 141.8, 138.9, 137.2, 136.9, 134.3, 132.4, 131.2, 130.4, 130.3, 129.0, 128.8, 128.5, 128.2, 128.0, 124.4, 123.2, 67.8, 21.3. FD-MS: *m*/*z* = 375.3. Anal. Calcd for $C_{28}H_{22}O_0$ (374.5): C, 89.81; H, 5.92. Found: C, 89.74; H, 5.88.

Acknowledgment. The authors would like to thank Prof. Dr. Klaus Müllen for generous support of this study. Financial support for H.A.R. was given by the Deutsche Forschungsgemeinschaft (DFG).

JO9817523

(9) Criegee, R.; Marchand, B.; Wannowius, A. *Liebigs Ann. Chem.* **1942**, *550*, 99.