A Versatile Synthetic Approach to Rhodium(III) Diimine Metallointercalators: Condensation of *o*-Quinones with Coordinated *cis*-Ammines

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A new route to the preparation of rhodium(III) diimine complexes which bind DNA by intercalation was developed by condensation of coordinated ammine ligands with *o*-quinones. Starting from *cis*-$[Rh(L\hat{}L)_2(NH_3)_2]^{3+}$ (L^L: 2,2′-bipyridine or 1,10-phenanthroline) and the appropriate quinones the ligands 9,10-phenanthrenequinone diimine (phi) and 5,6-chrysenequinone diimine (chrysi) were introduced in high yields. The reactions are completed within hours at ambient temperature in MeCN/water mixtures, 0.1 M in NaOH. Experiments with enantiomerically pure Δ-$[Rh(phen)_2(NH_3)_2]^{3+}$ and 9,10-phenanthrenequinone showed that the configuration at the metal center is retained during the course of the reaction. Condensation of rhodium(III) tetraammine starting material with 9,10-phenanthrenequinone allows the selective introduction of one or two phi ligands, depending on the reaction conditions. The ability to incorporate specifically only one phi ligand makes this a promising approach for the synthesis of tris(heteroleptic) coordination compounds, and one example of such a complex, $[Rh(phen)(phi)(chrysi)]^{3+}$, is provided.

Introduction

Our laboratory has focused on the construction of transition metal complexes which bind DNA with site specificity in order to explore systematically those factors which contribute to DNA site recognition.[1] Investigation has focused on 9,10-phenanthrenequinone diimine (phi) complexes of rhodium(III), which bind DNA avidly by intercalation from the major groove and, with photoactivation, promote DNA strand cleavage at their binding site.[2] These octahedral complexes are useful in probing nucleic acid structure and recognition owing to the kinetic inertness of the d^6 rhodium(III) center, the relative rigidity of the complexes, their high binding affinity to nucleic acids, and their rich photochemistry.

Various methods for the synthesis of phi complexes of rhodium(III) and ruthenium(II) have been described.[3] The common feature of these procedures is the coordination of 9,10-diaminophenanthrene to the metal center with subsequent oxidation of the coordinated ligand to the bis-diimine. An alternative approach for tris(phi) complexes consists of the *in situ* deprotection of bis(trimethylsilyl)phenanthrenequinone diimine in the presence of an appropriate metal precursor.[4] The main drawbacks of these protocols are their moderate to low yields and the requirement for anaerobic conditions during coordination. Also, the methodology is relatively limited, since the introduction of the intercalating diimine ligands relies on the synthetic availability of the appropriate 1,2-diamino precursors. This point proved to be crucial in our attempts to synthesize chrysenequinone diimine complexes of rhodium(III) for the selective recognition of mismatched base pairs in DNA.[5]

The condensation of primary amines with aldehydes and ketones is the method of choice to prepare Schiff bases.[6] The related condensation of *o*-quinones with aromatic *o*-amines has received increasing attention recently from different groups as a convenient way to create extended aromatic ligand systems for coordination compounds. Several reports describe the preparation of free ligands with subsequent coordination to metal centers.[7] Jonasdottir *et al.*[8] formed nickel(II) and cobalt(II) complexes by a metal template approach comprising the condensation of a bis-aldehyde with 1,2-diamino-4,5-dimethoxybenzene. Condensation of ruthenium(II) complexes of 1,10-phenanthroline-5,6-dione with the appropriate primary aromatic *o*-diamines was also employed[7c,9] to build extended aromatic

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systems directly on the metal center. Noteworthy is the observation that the reactions proceed with retention of the configuration at the metal center when enantiomerically pure dione starting material was used. Enantiomerically pure $[Ru(phen)_2(1,10\text{-phenanthroline-}5,6\text{-dione})]^{2+}$ and $[Ru(phen)_2(1,10\text{-phenanthroline-}5,6\text{-diamine})]^{2+}$ have been condensed to form dimeric ruthenium(II) species with retention of the configuration at the two metal centers.[10] Recently, the same group reported the first synthesis of chiral ruthenium(II) dendrimers based on the same condensation strategy.[11]

The formation of Schiff bases by condensations with aldehydes or ketones is not restricted to primary amines. The notion of forming Schiff base complexes and in fact using coordinated ammine ligands had its origins in the work of Sargeson and co-workers.[12] For example, they observed, that under strongly basic conditions, the pyruvatopentaamminecobalt(III) complex rearranges intramolecularly to form a coordinating imine.[12a]

On the basis of these results, we initiated studies of the condensation of *o*-quinones with *cis*-diammine rhodium(III) complexes under similar conditions. Our primary goal was to find an alternative, higher yielding synthetic route for the introduction of the phenanthrenequinone diimine (phi) ligand which is used extensively in our laboratory as a standard DNA intercalation moiety. In addition, we were interested in the intercalation properties of other extended aromatic ligands. Earlier protocols were of limited utility for such studies, since the synthesis of coordination compounds depended on the availability of the respective 1,2-diamino precursors. *O*-Quinones present viable alternatives since they are often synthetically easily accessible.[6b] For example, 5,6-chrysenequinone can be prepared from chrysene by oxidation with $K_2Cr_2O_7$.[13]

Here we report a more general synthetic approach for the introduction of intercalating ligands in rhodium(III) complexes starting from *o*-quinones and metal complexes with cis-coordinated amino ligands.

Experimental Section

Measurements and Materials. The NMR studies (^{1}H and ^{13}C NMR, 2D-COSY, ^{1}H^{13}C-HETCOR and decoupling experiments) were performed on a General Electric QE Plus 300 MHz instrument using solvent as the internal standard. Electronic spectra were measured on a Varian Cary 2200 and a Beckmann DU 7400 UV/vis spectrophotometer. Mass spectral data were collected at the mass spectra facilities of the University of California, Riverside, CA (FAB and electrospray), and at the Macromolecular Resources Center of Colorado State University, Department of Biochemistry, Fort Collins, CO (MALDI and electrospray). CD spectra were measured on a Jasco J-500A spectropolarimeter. High-performance liquid chromatography (HPLC) was carried out with a HP 1050 system on a Rainin Microsorb-MV C_{18} 100 Å column (1.0 mL/min liquid phase, linear gradient over 45 min from 0.1% trifluoroacetic acid in water to 100% acetonitrile). Thin-layer chromatography was conducted on silica gel IB-F plates (J. T. Baker).

Unless otherwise specified, commercial chemicals were used as supplied. $RhCl_3 \cdot 2H_2O$ was obtained from Johnson & Matthey or Aldrich, 9,10-phenanthrenequinone, (+)-KSb-tartrate, triflic acid, and Sephadex cation and anion exchange resins were from Aldrich, $[Rh(NH_3)_5Cl]Cl_2$ was from Pfaltz+Bauer, MeCN of spectroscopic quality was from Merck, and chrysene was from Acros Chemicals. d_8-2,2′-Bipyridine was kindly donated by P. Belser and A. von Zelewsky, Fribourg University, Fribourg, Switzerland. 5,6-Chrysenequinone[13] and $[Rh(NH_3)_6](CF_3SO_3)_3$[14] were prepared according to published procedures.

Synthesis and Characterization. ***rac*-[Rh(phen)$_2$(NH$_3$)$_2$](PF$_6$)$_3$.** Bis(ammine)bis(phenanthroline)rhodium(III) was prepared as described in the literature[15] with the following modifications: The chloride ligands of $[Rh(phen)_2Cl_2]Cl$ were substituted by stirring in neat triflic acid overnight.[16] The brownish solution was carefully introduced into chilled diethyl ether. The beige precipitate was separated either by centrifugation or by filtration, dissolved in concentrated ammonia solution, and refluxed for 15−30 min. The complex was precipitated as the PF_6 salt, and the counterion was exchanged to chloride on a Sephadex QAE-A25 anion exchange column and finally purified on a Sephadex SP-C25 cation exchange column by elution with 0.05 M $MgCl_2$ in MeCN/water, 1:1. The fractions containing the complex were identified by TLC, combined, concentrated, and precipitated as colorless crystals by the addition of NH_4PF_6. Yield: 53%.

^{1}H NMR (acetone-d_6, 300 MHz): δ 9.93 (2H, d), 9.42 (2H, d), 8.99 (2H, d), 8.64 (4H, m), 8.51 (2H, d), 8.32 (2H, d), 7.87 (2H, dd), 5.18 (6H, broad s). ^{13}C NMR (acetone-d_6, 75.44 MHz): δ 154.1, 153.6, 147.6 q, 146.6 q, 142.9, 141.5, 133.2 q, 129.2, 129.1, 128.3, 127.7. MS (electrospray): 645 (35, $M^+ - 2PF_6$), 495 (100, $M^+ - 3PF_6$); UV/vis (acetonitrile/water, 1:1, 1.905×10^{-5} M): 302 (12 400), 271 (51 500), 222 (51 800); $R_f = 0.45$ (silica gel, MeCN/water/*n*-butanol/KNO_3, 4:1:1:0.1).

Enantiomer Separation. A 150 mg sample of the racemic mixture was separated under dark room conditions on a 150 cm long (d =3 cm) Sephadex CM-C25 ion exchange column eluting with 0.15 M (+)-potassium antimonyl tartrate in water.[17] The column was washed with deionized water and then carefully blown out onto a flat surface. The resin was divided into 20 equally sized pieces and eluted individually in the dark with MeCN/water, 1:1. The fractions containing metal complex were identified by TLC. The Δ and Λ enantiomers were separated by six fractions containing no product, with the Λ enantiomer eluting faster. The Λ enantiomer fractions were reduced in volume on a rotary evaporator and then diluted to 250 mL. The Δ enantiomer fractions were brought to a total volume of 250 mL, and the concentration was determined in both cases by absorption spectroscopy. The $\Delta\epsilon$ values obtained for the Λ enantiomer are approximately 15% less than for the Δ sample, revealing that heating during rotary evaporation caused partial racemization.

Δ-[Rh(phen)$_2$(NH$_3$)$_2$]Cl$_3$. CD (acetonitrile/water, 1:1, 1.93×10^{-5} M): 225 (27), 266 (44), 280 (−80), 304 (−16).

Λ-[Rh(phen)$_2$(NH$_3$)$_2$]Cl$_3$. CD (acetonitrile/water, 1:1, 2.51×10^{-5} M): 227 (−19), 266 (−40), 280 (70), 303 (14).

[Rh(bpy)$_2$(NH$_3$)$_2$]Cl$_3$. The complex was synthesized according to the same procedure as described above for *rac*-$[Rh(phen)_2(NH_3)_2](PF_6)_3$ with the exception that instead of precipitation as the PF_6 salt the compound was isolated by evaporation. Yield: 94%.

^{1}H NMR (acetone-d_6, 300 MHz): δ 9.45 (2H, d), 9.05 (2H, d), 8.89 (2H, d), 8.79 (2H, td), 8.45 (2H, td), 8.30 (2H, td), 8.05 (2H, d), 7.74 (2H, td), 5.06 (6H, broad s). MS (electrospray): 449.0 (45, $M^+ -$

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3Cl), 447.1 (100, $M^+ - 3Cl - 2H$), 430.1 (45, $M^+ - 3Cl - NH_3$); $R_f = 0.04$ (silica gel, MeCN/water/*n*-butanol/KNO_3, 4:1:1:0.1).

[Rh(phen)(NH$_3$)$_4$]Cl$_3$. [Rh(phen)Cl_4](H_3O^+) was prepared as described in the literature.[18] The chloride ligands were exchanged to triflate by overnight treatment in neat triflic acid.[16] The brownish solution was carefully introduced in chilled diethyl ether. The beige precipitate was separated either by centrifugation or by filtration, dissolved in concentrated ammonia solution, and refluxed for 30 min. The solution was allowed to cool and was then evaporated to dryness.

^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.24 (2H, d), 9.03 (2H, d), 8.39 (2H, s), 8.27 (2H, m), 5.05 (6H, broad s), 4.04 (6H, broad s). MS (electrospray): 350.1 (32, $M^+ - 3Cl - H$), 349.4 (100, $M^+ - 3Cl - 2H$) 348.5 (70, $M^+ - 3Cl - 3H$).

Typical Reaction Conditions Starting from [Rh(phen)$_2$(NH$_3$)$_2$]$^{3+}$, [Rh(bpy)$_2$(NH$_3$)$_2$]$^{3+}$, and [Rh(phen)(NH$_3$)$_4$]$^{3+}$. In a typical preparation, 50 mg of Rh(III) starting material was dissolved in 32 mL of MeCN/water, 3:1, 0.1 M in NaOH. To this mixture was added 1 equiv or more of 9,10-phenanthrenequinone or 5,6-chrysenequinone. During constant stirring, the reaction was allowed to progress for approximately 18 h at room temperature. After neutralization with dilute hydrochloric acid and addition of 500 mL of water, the reaction mixture was loaded onto a Sephadex SP-C25 ion exchange column equilibrated in 0.05 M $MgCl_2$. The product was purified by elution with a gradient of 0.05−0.5 M $MgCl_2$, and the orange product bands were collected. The fractions were concentrated on a Waters Sep-Pak 5g C_{18} cartridge and washed with copious amounts of water. The metal complex was eluted from the cartridge with a minimum volume of 0.1% TFA in MeCN/water, 1:1, and lyophilized to dryness.

***rac*-[Rh(phen)$_2$(phi)]Cl$_3$.** This orange compound was prepared according to the outline above. Yield: 86%. The characterization data are in good agreement with data in the literature.[3b]

Δ-[Rh(phen)$_2$(phi)](PF$_6$)$_3$. Sodium hydroxide (0.6 g) was dissolved in 100 mL of MeCN/water, 1:1, containing Δ-[Rh(phen)$_2$(NH$_3$)$_2$]Cl_3 (18.4 mg, 0.037 mmol). 9,10-Phenanthrenequinone (8 mg, 0.038 mmol) in 50 mL of acetonitrile was added and the mixture stirred at room temperature. Aliquots (400 μL) were removed at intervals and mixed with 100 μL of 1.16 M HCl in MeCN/water, 1:1. These samples were subsequently analyzed by HPLC. After 1 day, the reaction mixture was neutralized with diluted hydrochloric acid and the volume reduced to approximately 20 mL. The complex was precipitated with 1 g of NH_4PF_6 and collected on Celite. The residue was dissolved in a minimum of acetonitrile and evaporated to dryness. Yield: 26.1 mg (64%). The characterization data (^{1}H NMR, MS, CD, UV/vis) agree well with published data,[19] with slightly higher $\Delta\epsilon$ values observed by CD spectroscopy.

CD (acetonitrile, 1.47×10^{-5} M): 261 (99), 275 (−179), 346 (−24).

***rac*-[Rh(bpy)$_2$(phi)](PF$_6$)$_3$.** This product was synthesized starting from [Rh(bpy)$_2$(NH$_3$)$_2$]$^{3+}$. The characterization data agree well with published data.[20]

***rac*-[Rh(bpy)$_2$(chrysi)]Cl$_3$.** [Rh(bpy)$_2$(NH$_3$)$_2$](PF$_6$)$_3$ (195.5 mg, 0.22 mmol) and 5,6-chrysenequinone (56.8 mg, 0.22 mmol) were dissolved with rapid stirring in 15 mL of acetonitrile under atmospheric conditions. Aqueous sodium hydroxide (5 mL, 0.4 M) was added and the reaction vessel capped to prevent evaporation. After 3 h the reaction was stopped by the addition of 5−6 mL of 0.4 M hydrochloric acid. The mixture was diluted, purified, and isolated as described above. Yield: 28 mg (83%).

^{1}H NMR (MeOH-d_4, 500 MHz): δ 8.94 (2H, t), 8.86 (2H, t), 8.80 (1H, d), 8.77 (1H, d), 8.56 (2H, split t), 8.44 (5H, m), 8.40 (1H, d), 8.15 (1H, m), 8.03 (1H, m), 7.95 (3H, m), 7.86 (1H, d), 7.81 (1H, d), 7.64 (5H, m). ^{13}C NMR (MeOH-d_4, 125.73 MHz): δ 183.3, 177.3, 175.4, 157.4, 157.2, 157.2, 153.8, 153.2, 152.1, 144.6, 144.5, 143.9, 143.8, 139.7, 138.8, 138.4, 136.2, 135.7, 132.3, 132.2, 132.0, 131.8, 130.9, 130.77, 130.6, 130.2, 129.4, 127.7, 127.6, 127.3, 126.9, 126.8, 123.9, 122.9, 120.8, 118.6, 116.3, 114.1. MS (FAB): 671 (24%, $M^+ - 3Cl$), 670.1 (63, $M^+ - 3Cl - H$), 669.1 (100, $M^+ - 3Cl - 2H$); UV/vis (water, 7.76×10^{-6} M): 303 (57 000), 315 (52 200), 391 (10 600). $\epsilon_{271\ nm}$: 63 800 M^{-1} cm^{-1} (pH isosbestic point); $R_f = 0.33$ (silica gel, MeCN/water/*n*-butanol/KNO_3, 4:1:1:0.1).

Enantiomeric Separation. The enantiomers of the complex were separated on a Sephadex SP-C25 column eluted with 0.15 M of (+)-KSb tartrate in water.[17] The separated orange fractions, with the Λ enantiomer being eluted faster, were collected and concentrated on a Waters Sep-Pak 5g C_{18} cartridge. After washing with water, the residue was dissolved in a minimum of MeCN/water, 1:1, and evaporated to dryness.

Δ-[Rh(bpy)$_2$(chrysi)]Cl$_3$. CD (water, 7.76×10^{-6} M): 233 (34), 264 (26), 286 (−12), 308 (−42), 318 (−100), 341 (6).

Λ-[Rh(bpy)$_2$(chrysi)]Cl$_3$. CD (water, 7.76×10^{-6} M): 233 (−34), 264 (−26), 286 (12), 308 (42), 318 (100), 341 (−6).

***rac*-[Rh(d_8-bpy)$_2$(chrysi)]Cl$_3$.** This complex was synthesized as above but with deuterated 2,2′-bipyridine.

***rac*-[Rh(phen)$_2$(chrysi)]Cl$_3$.** This compound was prepared analogously to *rac*-[Rh(bpy)$_2$(chrysi)] Cl_3. Yield: 77%.

***rac*-[Rh(phen)(phi)$_2$](PF$_6$)$_3$.** This orange compound was prepared from [Rh(phen)(NH$_3$)$_4$]Cl_3 with 2 equiv of 9,10-phenanthrenequinone following the outline above. The product was purified on a Sephadex SP-C25 cation exchange column eluting with 1.0 M $MgCl_2$ acidified with a few drops of diluted HCl. Yield: 54%. The characterization data are in good agreement with the literature.[20]

***rac*-[Rh(phen)(phi)(chrysi)]Cl$_3$.** [Rh(phen)(NH$_3$)$_4$](CF_3SO_3)$_3$ (17 mg, 0.021 mmol) was combined with 9,10-phenanthrenequinone (5.4 mg, 0.026 mmol) in acetonitrile (9.6 mL), water (2.0 mL), and NaOH solution (1.6 M, 1.2 mL). After 60 min of stirring at ambient temperature, 5,6-chrysenequinone (9.9 mg, 0.039 mmol) was added. The reaction was stopped after 20 h by neutralization with diluted hydrochloric acid. The product was purified on a Sephadex SP-C25 cation exchange column eluting with a gradient of 0.05−0.5 M $MgCl_2$. The red product band was collected, and the fractions were concentrated on a Waters Sep-Pak 5g C_{18} cartridge and washed with copious amounts of water. The metal complex was eluted from the cartridge with a minimum volume of 0.1% TFA in MeCN/water, 1:1, and lyophilized to dryness. Yield: 14 mg (75%).

^{1}H NMR (D_2O, 300 MHz): complicated multiplets centered at 8.94, 8.36, 8.08, 7.80, and 7.60. Integrals were consistent with the desired product.

MS (electrospray): 745.3 (18, $M^+ - 3Cl$), 744.3 (75, $M^+ - 3Cl - 1H$), 743.2 (100, $M^+ - 3Cl - 2H$).

Typical Reaction Conditions Starting from [Rh(NH$_3$)$_5$Cl]$^{2+}$ and [Rh(NH$_3$)$_6$]$^{3+}$. In a typical preparation 75 mg of Rh(III) starting material was dissolved in 75 mL of MeCN/water, 2:1, 0.1 M in NaOH. To this mixture was added 1, 2, or 3 equiv of 9,10-phenanthrenequinone. The mixtures were stirred at room temperature, and the progress of the reaction was monitored by HPLC. The reaction mixtures were neutralized with diluted HCl after all 9,10-phenanthrenequinone was consumed and the MeCN removed on a rotatory evaporator. Organic side products were extracted with dichloromethane and the mono- and bis(phi) complexes separated by preparative liquid chromatography.

Results and Discussion

Scheme 1 gives an overview of our synthetic approach starting from different *cis*-Rh(III) ammine complexes and 9,10-phenanthrenequinone (**A**) or 5,6-chrysenequinone (**B**), respectively. The following results illustrate the versatility of the condensation methodology for the preparation of a wide variety of intercalating octahedral metal complexes.

Starting from *cis*-[Rh(phen)$_2$(NH$_3$)$_2$]$^{3+}$ and *cis*-[Rh(bpy)$_2$(NH$_3$)$_2$]$^{3+}$. Mono(phi) and mono(chrysi) complexes can be synthesized starting from *cis*-diammine rhodium(III) compounds. The rhodium(III) complexes were prepared according to literature methods.[15] They were reacted at ambient temperature with either 9,10-phenanthrenequinone or 5,6-chrysenequinone in MeCN/water mixtures, 0.1 M in NaOH. The

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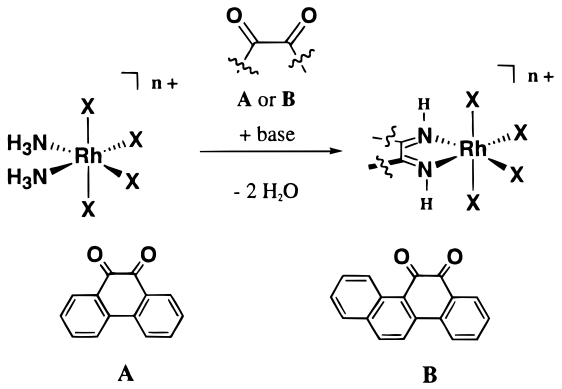
Scheme 1. Schematic Representation of the Condensation of *cis*-Ammine Rhodium(III) Complexes with 9,10-Phenanthrenequinone (**A**) and 5,6-Chrysenequinone (**B**)



progress of the reactions was monitored by HPLC. Figure 1 shows a representative set of HPLC traces for the condensation of $[Rh(phen)_2(NH_3)_2]Cl_3$ with 9,10-phenanthrenequinone. The clean and quantitative transformation of the two starting materials to a single product is evident from the lack of observable side products. On the basis of its characteristic absorbance spectrum, the peak at approximately 14 min was identified as the expected phi complex. Under the condensation conditions detailed in the Experimental Section, the reactions typically went to completion after stirring at ambient temperature for several hours. After the consumption of the starting materials, the reaction mixtures were neutralized and the complexes purified on cation exchange columns. Although the reactions proceeded quantitatively as monitored by HPLC, mechanical losses during workup account for the observed isolated yields. Overall, observed yields were far superior to those of alternative synthetic routes. The isolated products were characterized by NMR and other spectroscopic methods. The data obtained for all previously known coordination compounds are in good agreement with the literature.

The condensation procedure outlined above was used also to synthesize rhodium(III) complexes containing the new DNA intercalation ligand 5,6-chrysenequinone diimine (chrysi). Reaction of 5,6-chrysenequinone with *cis*-$[Rh(L^{\wedge}L)_2(NH_3)_2]^{3+}$ (L^L: 2,2′-bipyridine or 1,10-phenanthroline) readily produced the corresponding chrysi complexes in high yields. To assign completely the complicated pattern of resonances in the aromatic region of the ^{1}H NMR spectrum of $[Rh(bpy)_2(chrysi)]^{3+}$, the reaction was duplicated with fully deuterated 2,2′-bipyridine. Assessed by NMR, the d_8-bpy starting material had an isotopic purity ≥95%. A comparison of the aromatic region of the ^{1}H NMR spectrum of $[Rh(bpy)_2(chrysi)]^{3+}$ with $[Rh(d_8\text{-bpy})_2(chrysi)]^{3+}$ is depicted in Figure 2.

The enantiomers of $[Rh(bpy)_2(chrysi)]^{3+}$ were resolved on a cation exchange column eluted with 0.15 M (+)-KSb tartrate in water.[17] This resulted in two well-separated orange-brown bands with the Λ enantiomer being eluted faster. The CD spectra of the two enantiomers display the expected exact mirror image symmetry (Supporting Information). The configuration at the metal center was assigned using the exciton coupling model.[21] The recognition properties of these two enantiomers for mismatched DNA sequences is reported elsewhere.[5]

Reaction with Retention of the Configuration at the Metal Center. The mild reaction conditions prompted us to examine whether the condensation reaction proceeds with retention of the configuration at the metal center. The enantiomers of $[Rh(phen)_2(NH_3)_2]^{3+}$ were resolved on a cation exchange column eluted with 0.15 M of (+)-KSb tartrate in water,[17] with the Λ enantiomer being eluted faster. The configuration at the metal center was assigned using the exciton coupling model.[21] The CD spectra of the two enantiomers (Supporting Information) display the expected mirror image relationship.

Δ-$[Rh(phen)_2(NH_3)_2]^{3+}$ was reacted with 9,10-phenanthrenequinone at ambient temperature. The progress of the condensation was followed by HPLC. As with the racemic starting material, a clean transformation of Δ-$[Rh(phen)_2(NH_3)_2]^{3+}$ and 9,10-phenanthrenequinone was observed (Supporting Information). The reaction was also followed by absorption and CD spectroscopy (Figure 3). The absorption band centered at 379 nm characteristic of the phi ligand grows in over several hours and reaches a stable value after approximately 18 h. A control measurement after 3 days of reaction revealed no further change in the absorption features. The CD spectra of the starting material comprises a couplet in the ligand-centered transitions around 270 nm. As the condensation progresses, the overall shape of the two bands does not change. Only a moderate increase in the signal is observed, which can be attributed to the considerably enlarged aromatic system by the formation of the phi ligand. Furthermore, the CD spectra of the isolated

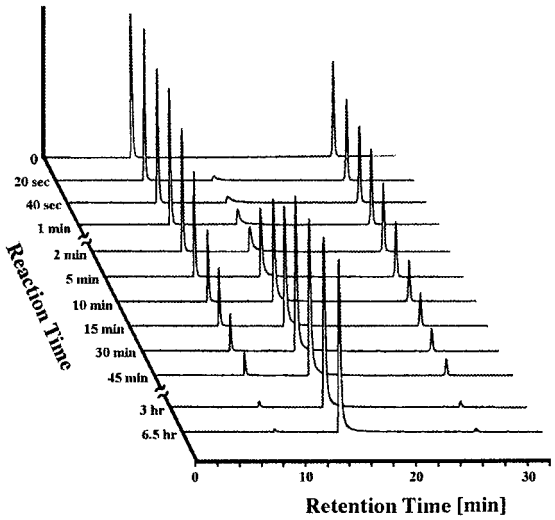


Figure 1. HPLC traces illustrating the clean conversion of $[Rh(phen)_2(NH_3)_2]^{3+}$ (1.7 mM; approximately 8 min) and equimolar 9,10-phenanthrenequinone (approximately 26 min) to $[Rh(phen)_2(phi)]^{3+}$ (approximately 14 min) in MeCN/water, 3:1, 0.1 M in NaOH at ambient temperature.

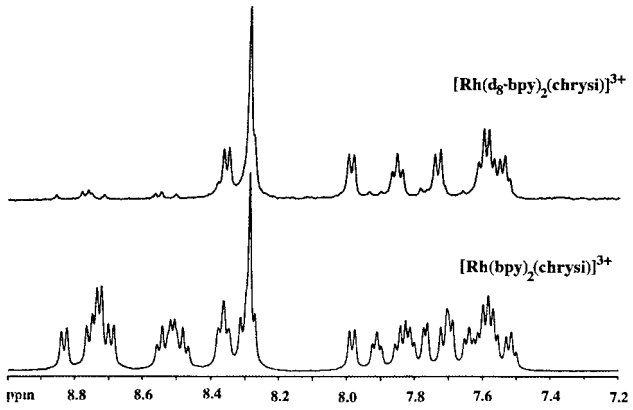


Figure 2. ^{1}H NMR spectra of $[Rh(d_8\text{-bpy})_2(chrysi)]^{3+}$ (top) and $[Rh(bpy)_2(chrysi)]^{3+}$ (bottom) measured in d_4-MeOH.

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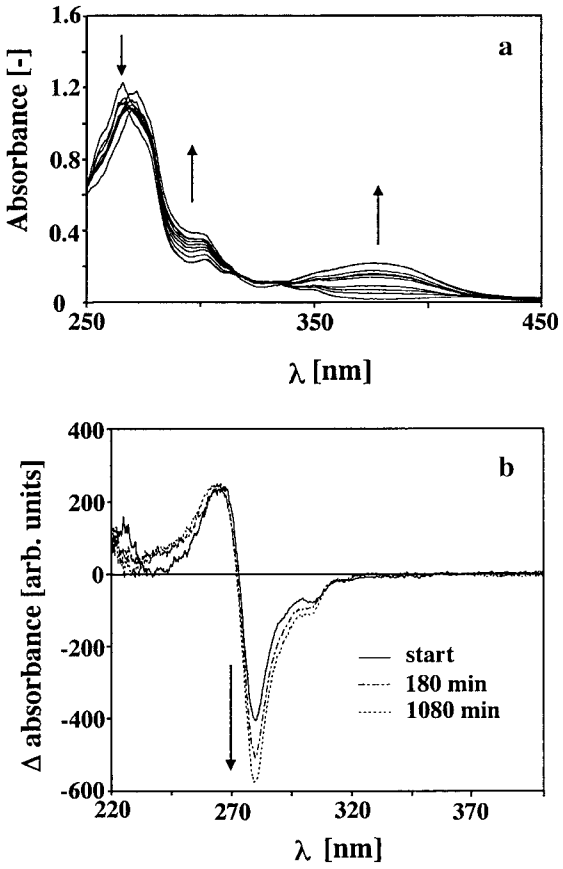

Figure 3. Condensation of Δ-$[Rh(phen)_2(NH_3)_2]^{3+}$ with 9,10-phenanthrenequinone followed (a) by UV/vis and (b) by CD spectroscopy.

product are identical to those of authentic Δ-$[Rh(phen)_2(phi)]^{3+}$ obtained by enantiomer separation on an ion exchange column.[19] These observations establish that no racemization occurs. The configuration at the metal center is retained during the course of the reaction. Enantiomerically pure *cis*-diammine complexes of rhodium(III) are therefore another example[22] of chiral building blocks which may have applicability in the stereoselective synthesis of transition metal complexes.

Formation of Bis(phi) and Tris(heteroleptic) Complexes from Tetraammine Starting Material. Starting from $[Rh(phen)(NH_3)_4]^{3+}$ and 2 equiv of 9,10-phenanthrenequinone, one or two phi ligands can be introduced. Figure 4 shows the HPLC traces for such an experiment. In the case shown, the stoichiometry of the starting materials is slightly deviated from a 1:2 metal to 9,10-phenanthrenequinone ratio. This explains the presence of unreacted mono(phi) complex after all quinone was consumed. At ambient temperature the incorporation of the first phi ligand is complete within a few minutes. The addition of the second phi ligand, resulting in a peak with a retention time of approximately 21 min, is considerably slower. It takes several hours to complete the second condensation step, which shows that there is an anticooperative effect of the first phi ligand. Overall, bis(phi) rhodium(III) complexes can be prepared in high

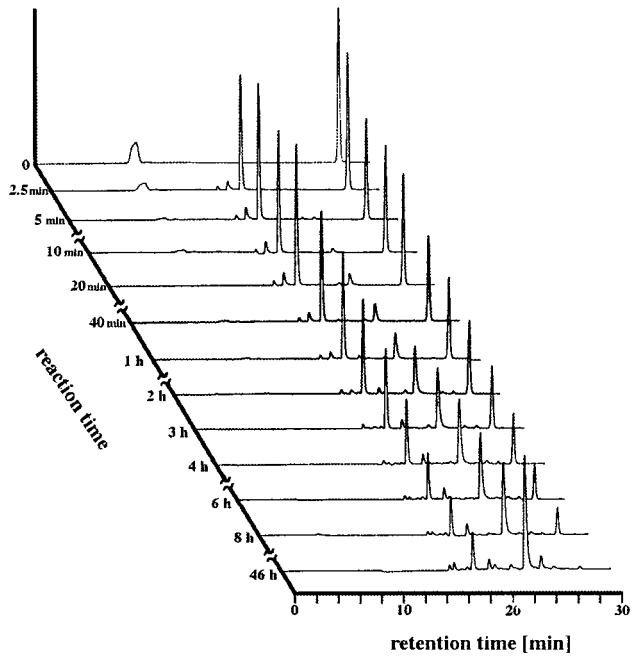

Figure 4. HPLC traces for the condensation of 2 equiv of 9,10-phenanthrenequinone with $[Rh(phen)(NH_3)_4]^{3+}$. Residual mono(phi) complex is present given less than stoichiometric quinone.

yields at ambient temperature by condensation of *o*-quinones with tetraammine starting material.

There is current interest in the generation of tris(heteroleptic) octahedral coordination compounds, and several synthetic procedures have been reported in the literature.[23] Given the anticooperativity in the formation of bis(phi) rhodium complexes, we studied the synthesis of three ligand compounds by sequential condensation of two different *o*-quinones with $[Rh(phen)(NH_3)_4]^{3+}$. But attempts to isolate the $[Rh(phen)(phi)(NH_3)_2]^{3+}$ intermediate from the reaction mixture and subsequent reaction of this product with an additional 1 equiv of *o*-quinone failed. Most likely, this is caused by the substitution of one of the ammine ligands of $[Rh(phen)(phi)(NH_3)_2]^{3+}$ during workup, leading to the loss of the strictly required *cis*-diammine moiety. This explanation is consistent with MS data of the isolated product, indicating the presence of a $[Rh(phi)(phen)(NH_3)(H_2O)]^{3+}$ species. If, however, the third ligand is introduced *in situ*, tris(heteroleptic) complexes of rhodium(III) are readily available in a one-pot reaction. Thus by addition of 1 equiv of 5,6-chrysenequinone to a reaction mixture of $[Rh(phen)(NH_3)_4]^{3+}$ and 9,10-phenanthrenequinone that was stirred under condensation conditions for 1 h, the expected $[Rh(phen)(phi)(chrysi)]^{3+}$ complex was formed. The isolated product has been characterized by MS and other spectroscopic methods. This proves that tris(heteroleptic) coordination compounds can indeed be synthesized by a sequential condensation approach.

Given the observed anticooperativity of the condensation reaction, an even more general procedure for the synthesis of three ligand complexes of the type $[Rh(phen)(phi)(L^{\wedge}L)]^{n+}$, where L^L is a bidentate chelate, can be envisioned. One phi ligand can be specifically incorporated in $[Rh(phen)(NH_3)_4]^{3+}$, followed by isolation of the mono(phi) intermediate. Subsequent introduction of L^L should allow the synthesis of a wide

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variety of tris-heteroleptic octahedral coordination compounds. Aquation of one of the ammine ligands in the $[Rh(phen)(phi)(NH_3)_2]^{3+}$ intermediate is of no importance in such a scenario, since aquo and hydroxy ligands are readily displaced by a wide variety of bidentate ligands.

Condensation Reactions with Pentaamine Starting Material. Starting from the commercially available $[Rh(NH_3)_5Cl]^{2+}$ the introduction of one or two phi ligands by condensation with 9,10-phenanthrenequinone was examined. The reaction proceeds considerably slower and less cleanly than in the experiments described above. Even after 6 days of stirring at ambient temperature, HPLC analysis showed the presence of sizable amounts of unreacted quinone starting material. The decomposition of 9,10-phenanthrenequinone to 9-hydroxy-9-carboxyfluorene[24] and other products in basic media becomes an important side reaction at these long reaction times. Nonetheless, mono- and bis(phi) complexes can still be isolated as the major products from the reaction mixtures.

Adding more base and increasing the concentrations of the starting materials resulted in no observable acceleration of the reaction. Only the ratio of mono- to bis(phi) complex produced after a given reaction time was shifted toward the bis(phi) complexes under more concentrated conditions. Raising the reaction temperature to 40 °C resulted in a considerable acceleration of both the condensation reaction and the decomposition of 9,10-phenanthrenequinone. Starting with 2 equiv of 9,10-phenanthrenequinone, more mono(phi) than bis(phi) complex is produced. This suggests that under these conditions the rate of decomposition of starting material is in the same regime as the second condensation step. Lowering the reaction temperature to 4 °C slowed the condensation considerably. Even after 13 days of reaction the starting materials were not entirely consumed. The decomposition of 9,10-phenanthrenequinone seems to be much more dependent on thermal activation than the condensation, since much smaller amounts of side products were observed in these experiments than at ambient temperature.

Attempted Formation of Tris(phi) Complexes from Hexaammine Starting Material. Starting from $[Rh(NH_3)_6]^{3+}$, the introduction of three phi ligands by condensation with 9,10-phenanthrenequinone was also studied. Overall, the same conclusions can be drawn as from experiments performed with $[Rh(NH_3)_5Cl]^{2+}$. Importantly, the sixth ammine ligand in $[Rh(NH_3)_6]^{3+}$ is known to be easily aquated under basic conditions.[25] The resulting $[Rh(NH_3)_5X]^{n+}$ ($X = H_2O$ or OH^-) lacks the required cis-arrangement of coordinated ammine ligands for the third condensation reaction to take place. This explains the predominance of mono- and bis(phi) products observed. HPLC analysis revealed only very small amounts of the tris(phi) complex formed under various reaction conditions. The condensation approach therefore is not a valid alternative for the synthesis of tris(phi) complexes. In such cases the older protocol[4] starting from bis(trimethylsilyl)phenanthrenequinone diimine proves to be more useful.

Conclusions

The condensation of *o*-quinones with rhodium(III) complexes containing two or four cis-coordinated ammine and either one or two 2,2′-bipyridine or 1,10-phenanthroline ligands proceeds rapidly, under very mild reaction conditions and in high yields. A wide array of *o*-quinones with extended aromatic systems either is commercially available or can be easily prepared. The condensation with coordinated ammine ligands represents a convenient method to introduce a variety of new intercalating ligands in coordination compounds. Given the anticooperativity of the second condensation reaction, this approach allows also the straightforward preparation of tris(heteroleptic) compounds. Moreover, no racemization at the metal center occurs during the course of the reaction. Potentially, all pure enantiomers of cis-bis and tetraamine metal complexes can thus be used as chiral building blocks.

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Supporting Information Available: CD spectra of the enantiomers of $[Rh(phen)_2(NH_3)_2]Cl_3$ and $[Rh(bpy)_2(chrysi)]Cl_3$ and HPLC traces depicting the progress of the condensation of 9,10-phenanthrenequinone with $[Rh(phen)(NH_3)_4]^{3+}$ and Δ-$[Rh(phen)_2(NH_3)_2]$, respectively (4 pages). Ordering information is given on any current masthead page.

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