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Rational Construction of Metallointercalators: Syntheses, Structures, and Characterizations of Isomers of ((2*S*,9*S*)-Diamino-4,7-diazadecane)(9,10-phenanthrenequinone diimine)rhodium(III)

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In an effort to design metallointercalators which bind DNA with predictable sequence specificity, a series of isomers of the complex $[Rh(Me_2trien)phi]^{3+}$ (Me_2trien = (2*S*,9*S*)- or (2*R*,9*R*)-2,9-diamino-4,7-diazadecane; phi = 9,10-phenanthrenequinone diimine) have been constructed. Here we report the synthesis and characterization of all six diastereomers (2α and 4β) of $[Rh[(S,S)\text{-}Me_2trien]phi]^{3+}$ (**1a–f**) and their enantiomers. The isomer distribution of products formed is found to depend on the reaction sequence used. Reaction of $RhCl_3$ with 9,10-diaminophenanthrene and then with (*S*,*S*)-Me_2trien followed by air oxidation results in no substantial formation of α-isomers. However reaction of $[Rh[(S,S)\text{-}Me_2trien]Cl_2]Cl$ with 9,10-diaminophenanthrene followed by air-oxidation yields about 30% α-isomers **1a** and **1d** (ratio 6:1). No asymmetric induction at the rhodium center is observed (ratio of Λ-isomers (**1a–c**) to Δ-isomers (**1d–f**) is 1:1). The diastereomers are separated by reversed-phase C_{18} HPL-chromatography. X-ray crystallography and base-catalyzed epimerization have been used to identify and characterize the isomers in detail. Crystal structures are reported for Λ,α-$[Rh[(2S,9S)\text{-}Me_2trien]phi](PF_6)_2Cl\cdot H_2O$ (monoclinic crystal system, space group $P2_1$, $Z = 2$, $a = 7.450(7)$ Å, $b = 21.347(6)$ Å, $c = 10.285(3)$ Å, $\beta = 95.92(5)°$, $V = 1627(2)$ Å^3), Λ,*anti*-β-$[Rh[(2S,9S)\text{-}Me_2trien]phi]Cl_3\cdot 3.9H_2O$ (monoclinic crystal system, space group $C2$, $Z = 4$, $a = 28.366(9)$ Å, $b = 10.317(4)$ Å, $c = 10.014(2)$ Å, $\beta = 90.71(2)°$, $V = 2930(4)$ Å^3), Λ,α-$[Rh[(2R,9R)\text{-}Me_2trien]phi](ClO_4)_3$ (monoclinic crystal system, space group $P2_1$, $Z = 4$, $a = 8.323(5)$ Å, $b = 18.432(16)$ Å, $c = 19.913(8)$ Å, $\beta = 90.46(4)°$, $V = 3055(3)$ Å^3), and Λ,*syn*-β-$[Rh[(2R,9R)\text{-}Me_2trien]phi][(+)\text{-}Sb\text{-}tartrate]_2ClO_4\cdot 8H_2O$ (triclinic crystal system, space group $P1$ (No. 1), $Z = 1$, $a = 11.303(3)$ Å, $b = 11.409(4)$ Å, $c = 11.875(4)$ Å, $\alpha = 92.69(3)°$, $\beta = 114.66(3)°$, $\gamma = 117.42(3)°$, $V = 1179.8(7)$ Å^3). Characteristic features of the ^1H NMR, UV/visible, and CD spectroscopic data provide a basis for the rapid assignment of absolute and relative configurations of complexes with the structure $[Rh(R_2trien)phi]^{3+}$.

Introduction

Studies in our laboratory have focused on the design of octahedral transition metal complexes which bind DNA with high sequence selectivity.[1] Toward that aim we have focused our attention recently upon phenanthrenequinone diimine (phi) complexes of rhodium which bind DNA by intercalation in the major groove.[2] Using the phi ligand as an anchor, which orients the complex with respect to the DNA groove, we may vary the stereochemistry and functionality on the ancillary nonintercalating ligands of the octahedral complex so as to position groups for optimum sequence-selective contacts with the DNA bases. Phi complexes of rhodium(III) furthermore promote DNA strand cleavage upon photoactivation. Hence specific sites recognized by the complexes may be easily discerned through high resolution studies of photoactivated cleavage on labeled DNA fragments. For example, recent DNA photocleavage studies with the complexes[3] $[Rh(NH_3)_4phi]^{3+}$, $[Rh(en)_2phi]^{3+}$, $[Rh([12]aneN_4)phi]^{3+}$, and $[Rh([12]aneS_4)phi]^{3+}$ show that $[Rh(NH_3)_4phi]^{3+}$, Δ-$[Rh(en)_2phi]^{3+}$, and $[Rh([12]aneN_4)phi]^{3+}$ bind primarily to 5′-GC-3′ sites through hydrogen-bonding interactions of the axial amines; $[Rh([12]aneS_4)phi]^{3+}$ binds at few sites owing to considerations of shape, and Λ-$[Rh(en)_2phi]^{3+}$ binds both 5′-GC-3′ sites through hydrogen bonding and 5′-TX-3′ sites owing to van der Waals interactions with the thymine methyl groups in the DNA groove.[4]

Control over coordination geometry and stereochemistry in the DNA-binding metal complex offers a means systematically to expand the repertoire of potential sites targeted on DNA. Photoactivated DNA cleavage has also been used to compare systematically the recognition characteristics of four C_2-symmetric isomers Λ,α-(*S*,*S*)-, Δ,α-(*S*,*S*)-, Λ,α-(*R*,*R*)-, and Δ,α-(*R*,*R*)-$[Rh(Me_2trien)phi]^{3+}$ (Me_2trien = 2,9-diamino-4,7-diazadecane, phi = 9,10-phenanthrenequinone diimine) and the parent complexes Λ- and Δ-$[Rh(en)_2phi]^{3+}$.[5] Using molecular modeling, the Δ,α-(*R*,*R*)-isomer was predicted to target selectively the four-base sequence 5′-TGCA-3′, and indeed photocleavage results demonstrated the preferential targeting of that site. As this example may illustrate, predictability in design requires a detailed understanding of the three-dimensional structure of the coordination complexes themselves in the absence of DNA.

Octahedral complexes containing the chiral tetradentate ligand (2*S*,9*S*)- or (2*R*,9*R*)-2,9-diamino-4,7-diazadecane (Me_2trien) can adopt different coordination geometries: trans, cis-α, and cis-β.[6] In the presence of a bidentate cis-chelating ligand, in our studies

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(1) (a) Pyle, A. M.; Barton, J. K. *Prog. Inorg. Chem.* **1990,** *38,* 413. (b) Sitlani, A.; Barton, J. K. *Handbook of Metal Ion Ligand Interactions in Biological Fluids,* Marcel Dekker Inc.: New York, 1994. (c) Chow, C. S.; Barton, J. K. *Methods Enzymol.* **1992,** *212,* 219.

(2) (a) David, S. S.; Barton, J. K. *J. Am. Chem. Soc.* **1993,** *115,* 2984. (b) Sitlani, A.; Long, E. C.; Pyle, A. M.; Barton, J. K. *J. Am. Chem. Soc.* **1992,** *114,* 2303. (c) Pyle, A. M.; Chiang, M.; Barton J. K. *Inorg. Chem.* **1990,** *29,* 4487.

(3) Krotz, A. H.; Kuo, L. Y.; Barton, J. K. *Inorg. Chem.* **1993,** *32,* 5963.

(4) Krotz, A. H.; Kuo, L. Y.; Shields, T. P.; Barton, J. K. *J. Am. Chem. Soc.* **1993,** *115,* 3877.

(5) Krotz, A. H.; Hudson, B. P.; Barton, J. K. *J. Am. Chem. Soc.* **1993,** *115,* 12577.

(6) Nomenclature: cis and trans refer to the relative positions at the octahedral rhodium center, Λ and Δ refer to the absolute configurations of the octahedral rhodium center, *R*,*S* to the absolute configurations of the tetrahedral carbon centers; α and β refer to the coordination geometries of the tetradentate ligand (α = C_2-symmetric, β = C_1-symmetric), syn/anti refers to the relative configurations at the secondary amine in the equatorial plane, and λ and δ refer to the chiral conformations of five-membered rings RhNCCN. Also ent-x describes the enantiomer of x, for which the structure is shown.

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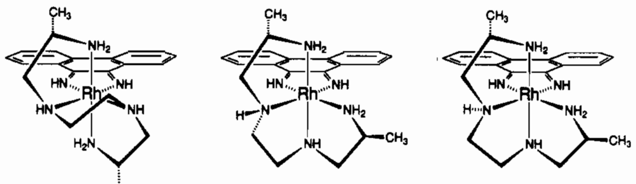
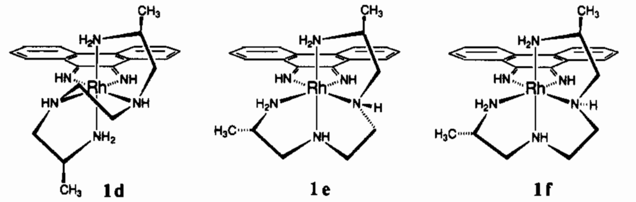


1a (S,S)-Λ,α **1b** (S,S)-Λ,anti-β **1c** (S,S)-Λ,syn-β



1d (S,S)-Δ,α **1e** (S,S)-Δ,anti-β **1f** (S,S)-Δ,syn-β

Figure 1. Six diastereomers of $[Rh[(S,S)\text{-}Me_2trien]phi]^{3+}$.

9,10-phenanthrenequinone diimine (phi), only cis-arrangements have to be considered. The six possible diastereomers $[Rh[(S,S)\text{-}Me_2trien]phi]^{3+}$ are shown schematically in Figure 1. There are two diastereomeric C_2-symmetric α-isomers **1a** (Λ,α) and **1d** (Δ,α) due to two chiral configurations at the rhodium center. The absolute configuration at the rhodium determines and limits the configurations of the chiral secondary amines in the equatorial plane. Four β-isomers, **1b**, **1c**, **1e**, and **1f** (Λ,*anti-β*; Λ,*syn-β*; Δ,*anti-β*, and Δ,*syn-β*), have to be considered due to the two chiral configurations at the rhodium and to two relative configurations (anti/syn) of the secondary amine in the equatorial position. In *anti-β*-isomers **1b** and **1e** the hydrogen atom of this secondary amine is directed away from the phi ligand; in *syn-β*-isomers **1c** and **1f**, it is directed toward the phi ligand. Modeling suggests that epimerization of these chiral nitrogens is not restricted by the β-geometry; however, conformational constraints and inter-ring repulsions will determine the syn/anti ratio for each of the two chiral configurations at the rhodium center. The chiral conformations (λ, δ) of the five-membered chelate rings N_{ax}–C–C–N_{eq}–Rh are largely determined by the tendency of the CH_3 groups to occupy equatorial positions.[7]

Here we report the synthesis and structural characterization of all six diastereomers of $[Rh[(S,S)\text{-}Me_2trien]phi]^{3+}$ (**1a–f**) and their enantiomers. Given the generality of the synthesis starting from the condensation of protected amino acids with ethylene diamine, a whole family of phi complexes of rhodium(III) containing the $[Rh(en)_2phi]^{3+}$ skeleton may be produced with a range of amino acid side chain functionalities arranged in different positions in space relative to the phi ligand. This construction should then provide an array of complexes for sequence-selective binding to DNA. For these studies to be fruitful, we require an unambiguous stereochemical characterization of at least one set of complexes in such a family using X-ray crystallography and the ability to extend the stereochemical assignments to other complexes in the series using spectroscopic methods, as provided herein. In addition, since C_2-symmetric complexes are preferred for sequence-selective binding to DNA, one synthetic goal was to find conditions under which a sufficient amount of the C_2-symmetric α-isomers are formed. Furthermore these studies provide an opportunity to compare and contrast the stability of an isomeric series of coordination complexes with α- and β-chelate configurations.

Experimental Section

Materials. (D)- and (L)-*N*-(Benzyloxycarbonyl)alanine were purchased from Sigma Chemical Co., isobutylchloroformate, BH_3·THF (1 M solution in THF), 9,10-diaminophenanthrene and Pd/C catalyst were purchased from Aldrich, and rhodium trichloride was purchased from Johnson Matthey Electronics. Ethylenediamine (Mallinckrodt) was distilled prior to use. THF was dried over sodium and benzophenone. Buffer pH 10 was purchased from Fisher Scientific. (2*S*,9*S*)-2,9-Diamino-4,7-diazadecane tetrahydrochloride ((*S*,*S*)-Me_2trien·4HCl) and the enantiomeric compound were synthesized as described earlier,[8] but with a slight modification. The deprotection of the amino groups was accomplished by catalytic (Pd/C) hydrogenation.

^1H NMR (300 MHz, D_2O), δ (ppm): 1.25 (d, $J = 6.7$ Hz, 6H, CH_3), 3.21 (AB of ABX, $J_{AB} = 13.1$ Hz, $J_{AX} = 6$ Hz, $J_{BX} = 7.2$ Hz, 4H, CH_2CH), 3.40 (s, 4H, CH_2CH_2), 3.63 (ddq, 2H, $CHCH_3$). ^{13}C NMR (75.47 MHz, D_2O), δ (ppm): 16.1, 44.0, 44.5, 50.4. $[Rh[(S,S)\text{-}Me_2trien]Cl_2]Cl$ was synthesized as described.[9]

Instrumentation. Fourier-transformed ^1H NMR spectra were taken with a JEOL GX-400 spectrometer at 400 MHz or with a General Electrics QE-300 spectrometer at 300 MHz in D_2O (referenced to 4.65). UV/visible spectra were recorded on a Cary 2200 spectrophotometer, and circular dichroism spectra, on a JASCO J-600 spectropolarimeter. Samples for CD spectroscopy were collected directly from the HPLC. Δε was calculated from the ellipticity according to the formula Δε [$cm^2\ dmol^{-1}$] $= \theta_\lambda \times 100/(c \times l \times 3298)$ using ellipticity θ_λ (deg), concentration c (mol/L) and cell length l (cm). High-performance liquid chromatography (HPLC) was carried out using a Waters 484 Tunable Absorbance Detector and a VYDAC Protein & Peptide C_{18} column. Peaks were detected by UV absorption at $\lambda = 254$ nm.

Measurement of pH-Dependent Optical Changes. An aqueous solution of the rhodium complex (50 μM) in water (20 mL) was brought to pH 2.5 by addition of hydrochloric acid. The solution was stirred vigorously, and the pH was monitored with a pH meter. After addition of aliquots of 1, 0.1, or 0.01 N aqueous sodium hydroxide, the pH was recorded and 1 mL was withdrawn for recording the UV/vis spectrum. After scanning, the solution was returned to the remaining 19 mL of solution and the cycle was repeated in order to monitor spectral changes at pH intervals of approximately 0.3 pH unit up to pH 11. In order to ensure that the changes were reversible, the pH was then lowered to the starting pH and the spectra were compared.

Ferrioxalate Actinometry. Ferrioxalate actinometry[10] was used to calibrate the photon flux from the He/Cd laser. Photon flux was calibrated before every photolysis experiment, by using three trials and a control at the irradiation wavelength of 325 nm. With our irradiation geometry, the photon flux value was 1.9×10^{-6} einstein/min.

Synthesis. (2*S*,9*S*)-2,9-(Diamino-4,7-diazadecane)(9,10-phenanthrenequinone diimine)rhodium(III) Trichloride, $[Rh[(S,S)\text{-}Me_2trien]phi]Cl_3$ (1a–f). Method A. Under nitrogen atmosphere, a mixture of $RhCl_3$ hydrate (100 mg, 0.44 mmol) and 9,10-diaminophenanthrene (93 mg, 0.45 mmol) in 3 mL of water was heated at reflux for 1 h. After the mixture was cooled to room temperature, 20 mL of dioxygen-free DMF was added. The mixture was filtered under nitrogen atmosphere into a degassed solution of (*S*,*S*)-2,9-diamino-4,7-diazadecane tetrahydrochloride (141 mg, 0.44 mmol) in 2 mL of 1 N aqueous NaOH. The solution was stirred for 10 min at room temperature and then added to 100 mL of 0.1 N hydrochloric acid and stirred under exposure to air for 24 h. The mixture was filtered and purified by Sephadex cation exchange chromatography (first with 0.2 N HCl and then eluted with 0.6 N HCl). Yield: 45%. According to HPLC less than 2% α-isomers formed; the ratio (**1e** + **1f**)/(**1b** + **1c**) = 50:50.

Method B. All operations were performed under rigorous exclusion of air. The reaction mixtures were degassed by three consecutive pump and saturate cycles with N_2. A solution of $[Rh[(S,S)\text{-}Me_2trien]Cl_2]Cl$ (130 mg, 0.35 mmol) in 0.7 mL of 2 N aqueous NaOH was heated at reflux for 30 min. After this mixture was cooled to room temperature, the pH was adjusted to 6 by dropwise addition of 0.5 M perchloric acid. This solution was added to a degassed suspension of 9,10-diaminophenanthrene (94 mg, 0.45 mmol) and 460 mg of sodium perchlorate in 1.5 mL of ethanol using a gastight syringe. The heterogeneous reaction mixture was heated at reflux for 3 h and cooled to room temperature, and after 50 mL of water was added, it was allowed to air oxidize overnight. After filtration and repeated extraction of the solid with water, the solutions were combined and purified by cation exchange chromatography

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(7) Corey, E. J.; Bailar, C. J. *J. Am. Chem. Soc.* **1959**, *81*, 2620.

(8) (a) Komorita, T.; Shimura, Y. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1832. (b) Muir, M. M.; Rechani, P. R.; Diaz, J. A. *Synth. React. Inorg. Met.-Org. Chem.* **1981**, *11*, 317.

(9) Muir, M. M.; Torres, L. M.; Zinner, L. B. *Synth. React. Inorg. Met.-Org. Chem.* **1987**, *17*, 221.

(10) Calvert, J. G.; Pitts, J. N. *Photochemistry;* John Wiley and Sons: New York, 1967.

Table 1. Crystallographic Data for Phi Complexes of Rh(III)

	1a-$Cl(PF_6)_2 \cdot 2H_2O$	**1b**-$Cl_3 \cdot 3.9H_2O$	**ent-1d**-$(ClO_4)_3$	**ent-1f**-[(+)-Sb-tartrate]$_2ClO_4 \cdot 8H_2O$
empirical formula	$C_{22}H_{36}ClF_{12}N_6O_2P_2Rh$	$C_{22}H_{39.8}Cl_3N_6O_{3.9}Rh$	$C_{22}H_{32}Cl_3N_6O_{12}Rh$	$C_{30}H_{52}ClN_6O_{24}RhSb_2$
fw	844.84	660.06	781.79	1262.62
crystal system	monoclinic	monoclinic	monoclinic	triclinic
space group	$P2_1$	$C2$	$P2_1$	$P1$ (No. 1)
a, Å	7.450(7)	28.366(9)	8.323(5)	11.303(3)
b, Å	21.347(6)	10.317(4)	18.432(16)	11.409(4)
c, Å	10.285(3)	10.014(2)	19.913	11.875(4)
α, deg				92.69(3)
β, deg	95.92(5)	90.71(2)	90.46(4)	114.66(3)
γ, deg				117.42(3)
V, Å^3	1627(2)	2930(4)	3055(3)	1179.8(7)
Z	2	4	4	1
d_{exp}, g cm^{-3}	1.72	1.50	1.69	1.78
μ(Mo Kα), cm^{-1}	7.95	8.84	8.80	16.24
cryst size, mm	0.18 × 0.20 × 0.43	0.56 × 0.27 × 0.22	0.025 × 0.19 × 0.43	0.19 × 0.22 × 0.23

(Sephadex SP C-50 (40–120 μm)). After elution with 0.1 M aqueous sodium chloride (100 mL) a red band was eluted with 0.3 M sodium chloride. The course of the chromatography was monitored by UV/vis spectroscopy (UV$_{max}$ at ca. 380 nm). The product fractions were evaporated to dryness and repeatedly extracted with dry ethanol to separate the product from the sodium chloride. Yield: 100 mg (50%) of a mixture of six diastereomeric compounds [Rh((*S*,*S*)-Me_2trien)phi]Cl_3 (**1a–f**). For analytical purposes the complexes were recrystallized from $NaClO_4$ solution. Anal. Calcd for [Rh(*S*,*S*)-Me_2trien)phi]$(ClO_4)_3 \cdot 3H_2O$ (fw 835.83): C, 31.61; H, 4.58; N, 10.05. Found: C, 31.71; H, 4.17; N, 10.12.

The isomers were separated by C_{18}-reversed-phase HPLC in three steps (A–C). Step A: mixture of all six isomers, eluent $CH_3CN/H_2O/TFA$ = 13:87:0.1; f = 7.0 mL/min; t_0 = 1.8 min, t_r(**1e**) = 9.4 min (0.6%), t_r(**1b**) = 10.4 min (14%), t_r(**1c,d,f**) = 12.8 min (61%), t_r(**1a**) = 14.6 min (23%). Step B: mixture of **1c–e**; eluent $MeOH/H_2O/TFA$ = 20:80:0.1; f = 4.5 mL/min; t_0 = 3.0 min, t_r(**1d**) = 28 min (6%), t_r(**1c,f**) = 32 min (94%). Step C: mixture of **1c,f**; eluent $CH_3CN/H_2O/TFA$ = 11:89:0.1; f = 9.0 mL/min; t_0 = 1.0 min, t_r(**1f**) = 26 min (87%), t_r(**1c**) = 27 min (13%).

Λ,α-[([2*S*,9*S*]-2,9-Diamino-4,7-diazadecane)(phenanthrenequinone diimine)rhodium(III)] (1a). ^{1}H NMR (D_2O, 400 MHz), δ: 8.25 (d, 2H), 8.17 (d, 2H), 7.71 (dd, 2H), 7.52 (dd, 2H), 2.4–3.6 (m, 10H), 1.07 (d, 6H). UV (λ_{max} [nm] (ϵ [M^{-1} cm^{-1}])): in water pH 7, 386 (sh, 12 500), 373 (13 500), 284 (sh, 11 800), 271 (25 700), 264 (sh, 22 200), 253 (17 800); in water pH 11, 372 (sh, 8600), 362 (8800), 283 (sh, 15 600), 273 (26 900), 265 (27 100); isosbestic points, 338 (5400), 292 (8900), 271 (25 500). CD ($\Delta\epsilon$ [cm^2 dmol^{-1}] (λ, [nm]) in CH_3CN, H_2O, TFA = 13:87:0.1: 3.1 (388), 3.0 (380), 9.2 (313), 0 (292), –8.8 (273).

Λ,*anti*-β-[([2*S*,9*S*]-2,9-Diamino-4,7-diazadecane)(phenanthrenequinone diimine)rhodium(III)] (1b). ^{1}H NMR (D_2O, 400 MHz), δSPCLN 8.50 (d, 1H), 8.18 (m , 3H), 7.70 (m, 2H), 7.50 (m, 2H), 3.0–3.6 (m, 10H), 1.30, 1.09 (2d, 6H). UV (λ_{max} [nm] (ϵ [M^{-1} cm^{-1}])): in water pH 2.5, 386 (sh, 12 500), 373 (13 500), 284 (sh, 11 800), 271 (25 700), 264 (sh, 22 200), 253 (17 800). CD ($\Delta\epsilon$ [cm^2 dmol^{-1}] (λ, [nm]) in CH_3CN, H_2O, TFA = 13:87:0.1: 2.8 (373), 0 (303), –1.7 (272).

Λ,*syn*-β-[([2*S*,9*S*]-2,9-Diamino-4,7-diazadecane)(phenanthrenequinone diimine)rhodium(III)] (1c). ^{1}H NMR (D_2O, 400 MHz), δ: 8.2 (m, 4H), 7.7 (m, 2H), 7.5 (m, 2H), 2.4–3.7 (m, 10H), 1.3, 1.1 (2d, 6H). UV (λ_{max} [nm] (ϵ [M^{-1} cm^{-1}])): in water pH 2.5, 386 (15 500), 285 (sh, 11 300), 271 (25 800), 264 (22 300), 252 (19 000). CD ($\Delta\epsilon$ [cm^2 dmol^{-1}] (λ, [nm]) in CH_3CN, H_2O, TFA = 13:87:0.1: 4.7 (372), 0 (283), –3.9 (272).

Δ,α-[([2*S*,9*S*]-2,9-Diamino-4,7-diazadecane)(phenanthrenequinone diimine)rhodium(III)] (1d). ^{1}H NMR (D_2O, 400 MHz), δSPCLN 8.18 (m, 4H), 7.70 (dd, 2H), 7.51 (dd, 2H), 2.45–3.65 (m, 10H), 1.00 (d, 6H). UV (λ_{max} [nm] (ϵ [M^{-1} cm^{-1}])): in water pH 7, 386 (sh, 12 500), 373 (13 500), 284 (sh, 11 800), 271 (25 700), 264 (sh, 22 200), 253 (17 800); in water pH 11, 372 (sh, 8600), 362 (8800), 283 (sh, 15 600), 273 (26 900), 265 (27 100); isosbestic points, 338 (5400), 292 (8900), 271 (25 500). CD ($\Delta\epsilon$ [cm^2 dmol^{-1}] (λ, [nm]) in CH_3CN, H_2O, TFA = 13:87:0.1: –2.0 (413), 0 (380), –14.8 (306), 0 (282), 9.2 (272).

Δ,*anti*-β-[([2*S*,9*S*]-2,9-Diamino-4,7-diazadecane)(phenanthrenequinone diimine)rhodium(III)] (1e). ^{1}H NMR (D_2O, 400 MHz), δSPCLN 8.51 (d, 1H), 8.20 (m, 3H), 7.72 (m, 2H), 7.52 (m, 2H), 2.7–3.7 (m, 10H), 1.40, 1.19 (2d, 6H). UV (λ_{max} [nm] (ϵ [M^{-1} cm^{-1}])): in water pH 2.5, 386 (15 500), 285 (sh, 11 300), 271 (25 800), 264 (22 300), 252 (19 000). CD ($\Delta\epsilon$ [cm^2 dmol^{-1}] (λ, [nm]) in CH_3CN, H_2O, TFA = 13:87:0.1: –3.3 (380), –9.7 (307), 0 (279), 4.5 (271).

Δ,*syn*-β-[([2*S*,9*S*]-2,9-Diamino-4,7-diazadecane)(phenanthrenequinone diimine)rhodium(III)] (1f). ^{1}H NMR (D_2O, 400 MHz), δ: 8.19 (m, 4H), 7.72 (m, 2H), 7.52 (m, 2H), 2.7–3.7 (m, 10H), 1.12, 1.38 (2d, 6H). UV (contains about 3% **1e**) (λ_{max} [nm] (ϵ [M^{-1} cm^{-1}])): in water pH 7, 386 (15 500), 285 (sh, 11 300), 271 (25 800), 264 (22 300), 252 (19 000); in water pH 11, 372–381 (br, 10 400), 285 (sh, 13 400), 273 (25 000), 265 (26 300); isosbestic points, 350 (6900), 269 (24 200). CD ($\Delta\epsilon$ [cm^2 dmol^{-1}] (λ, [nm]) in CH_3CN, H_2O, TFA = 13:87:0.1: –3.4 (380), –6.7 (307), 0 (285), 4.1 (272) .

(2*R*,9*R*)-2,9-(Diamino-4,7-diazadecane)(9,10-phenanthrenequinone diimine)rhodium(III) Trichloride, [Rh[(*R*,*R*)-Me_2trien]phi]Cl_3 (ent-1a–ent-1f). The ligand (2*R*,9*R*)-diamino-4,7-diazadecane was synthesized starting from *N*-Cbz-(D)-alanine. The same protocol as described above was used for the synthesis (method B) and chromatographic separation of the Rh(III) complexes.

Single-Crystal X-ray Diffraction Structural Characterization. Crystal structures of four complexes of different diastereomers of the cation with the molecular formula [Rh(Me_2trien)phi]$^{3+}$ have been obtained. Two isomers (**1a,b**) containing the (*S*,*S*)-Me_2trien ligand derived from L-alanine and two isomers containing (*R*,*R*)-Me_2trien derived from D-alanine (**ent-1d** and **ent-1f**) have been characterized in the solid state. Crystals were obtained by slow evaporation of HPLC-purified diastereoisomers from aqueous solutions containing the appropriate salt.

All X-ray crystallographic studies were done by using an Enraf-Nonius CAD-4 diffractometer. Data were collected for all structures at ambient temperature (22 ± 1 °C) with a ω scan mode using graphite-monochromated molybdenum radiation (λ(Kα) = 0.710 73 Å). The crystal data are summarized in Table 1. Hydrogen atoms were placed by calculation with d_{C-H} or d_{N-H} = 0.95 Å. The weights were taken as $1/\sigma^2(F_o^2)$. Variances ($\sigma^2(F_o^2)$) were derived from counting statistics plus an additional term, $(0.014I)^2$; variances of merged data were obtained by propagation of error plus another additional term, $(0.014I)^2$. Atomic scattering factors and dispersion correction were taken as described.[11] The programs used were those of the CRYM crystallographic computing system.[12]

Final heavy atom parameters, assigned hydrogen atom parameters, anisotropic displacement parameters, and complete distances and angles, respectively, are provided as supplementary material.

Structural Determination of Λ,α-[Rh[(*S*,*S*)-Me_2trien]phi]$Cl(PF_6)_2 \cdot 2H_2O$ (1a-$Cl(PF_6) \cdot 2H_2O$). A thick red needle was obtained from an aqueous solution of **1a**-Cl_3 and KPF_6 by slow evaporation at room temperature. It was cut to 0.43 mm long. A total of 25 reflections with $28° < 2\theta < 31°$ were used to determine the cell dimensions. An empirical absorption correction based on ψ scans was applied to the data set. The maximum and minimum relative transmission factors were 0.969 and 1.026, respectively. Data were collected from h = 0 to 8, k = –25 to +25 and l = –12 to +12; $((\sin\theta)/\lambda)_{max}$ was 0.59. Three standard reflections (033,

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(11) (a) Cromer, D. T.; Waber, J. T. *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IV, p 99. (b) Cromer, D. T. *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IV, p 149.

(12) (a) Duchamp, D. J. Presented at the American Crystallographic Association Meeting, Bozeman, MT, 1964; Paper B14, p 29. (b) Johnson, C. K. *ORTEPII*; 1976, Report ORNL-3794; Oak Ridge National Laboratory: Oak Ridge, TN, 1976.

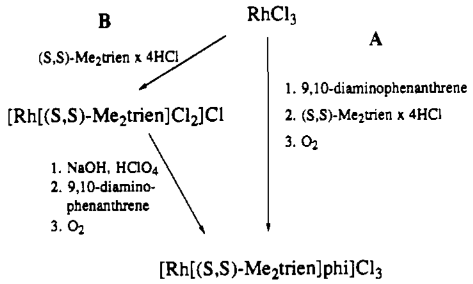
143 and *232*) showed no variation greater than those expected from counting statistics. A total of 6504 reflections were measured, and 2937 were independent (52 reflections were deleted because of background overlap). The goodness of fit for merging was 1.18; R_{int} = 0.025 for 2390 reflections with exactly two observations. All reflections were used in solution and refinement of the structure. Rhodium atom coordinates were found from the Patterson map, and remaining atoms, by a tedious series of structure factor–Fourier calculations. The *F* atoms were particularly difficult to find, but after some refinement of the Rh and P parameters they were evident in difference maps. R = 0.044 for 2582 reflections with $F_o^2 > 3\sigma(F_o^2)$, R_w on F^2 = 0.010, and R = 0.049 for 2874 reflections with $F_o^2 > 0$, R_w on F^2 = 0.010, and S = 1.65 for 2937 reflections and 414 parameters. In the final cycle, the $(\Delta/\sigma)_{max}$ ratio was 0.03 for all but F atoms, where the maximum was 0.21. Peaks in the final difference map of +0.62 and –0.57 e Å^{-3} were all near F atoms or water O atoms. No secondary extinction correction was used.

Structural Determination of Λ,*anti*-β-[Rh[(*S,S*)-Me$_2$trien]phi]Cl$_3$·3.9H$_2$O (1b-Cl$_3$·3.9H$_2$O). An orange-brown diamond-shaped prism was obtained from an aqueous solution of **1b**-Cl$_3$ and NaCl at 4 °C after several weeks. A total of 25 reflections with 26° < 2θ < 32° were used to determine the cell dimensions. An empirical absorption correction based on ψ scans was applied to the data set. The maximum and minimum relative transmission factors were 1.000 and 0.928. Data were collected from h = –30 to +30, k = –11 to +11 and l = 0 to +10. A total of 5752 reflections were measured to $((\sin\theta)/\lambda)_{max}$ = 0.54; 5146 were independent and used in the following calculations. Three standard reflections (every 2.5 h) showed no variations greater than those expected from counting statistics. For the solution and preliminary refinement of the structure, the intensities ($\pm h,\pm k,l$) were averaged according to Laue symmetry $2/m$ (S = 1.29 for 2428 multiple measurements, R_{merge} = 0.020 for 2223 duplicates). Coordinates of Rh and of one Cl atom (to break the $C2/m$ symmetry) were recovered from a Patterson map, and the remaining heavier atoms, from Fourier syntheses. When the model was nearly complete, the intensity data were reaveraged according to symmetry 2 (S = 1.06 for 316 multiple measurements, R_{merge} = 0.011 for 304 duplicate $h0l$'s), and parallel least-squares refinements were carried out for both chiralities; the correct one (known from synthesis) was clearly preferable, with R and S being about 10% smaller. The final refinement was based on 332 parameters. The final R was 0.0326 for the 5077 reflections with positive net intensity, and S was 1.90 for all 5141 reflections. The maximum shift was 0.18σ, for U_{33} of W(2); except for the water molecules, no shift was greater than 0.02σ.

Structural Determination of Λ,α-[Rh[(*R,R*)-Me$_2$trien]phi](ClO$_4$)$_3$ (ent-1d-(ClO$_4$)$_3$). A thin orange plate was obtained from an aqueous solution of **ent-1d**-Cl$_3$ and NaClO$_4$ by slow evaporation at room temperature. A total of 24 reflections with 20° < 2θ < 26° were used to determine the cell dimensions. No absorption correction was applied to the data set. Data were collected from h = –8 to +8, k = –17 to +17 and l = 0 to +19. Three standard reflections (every 2.5 h) showed no variation greater than those expected from counting statistics. A total of 6190 reflections were measured to $((\sin\theta)/\lambda)_{max}$ = 48.1 Å^{-1}; 2954 were independent in Laue symmetry $2/m$ and 5337 in 2, which were all considered observed and used in solution and refinement of the structure. The data were originally averaged in point group $2/m$ and the structure was solved and refined with those data. The data were reaveraged in point group 2 and the structure refined with $\Delta f''$ positive and negative. The positive values gave slightly better values of R and S, and that configuration agreed with the configuration known from the synthesis. The perchlorate anions, as usual, were not well-defined. Oxygen O(1) on Cl(1) shows a mean displacement of 0.71 Å, but we left it as a single atom. The oxygen atoms about Cl(6) are so poorly defined that we cannot construct a perchlorate group there: we modeled it as two half-populated Cl sites with fixed isotropic thermal parameters spaced (after refinement) 0.89(3) Å apart, with 12 oxygen atom sites whose populations, based on their height on a difference map, ranged from 0.70 to 0.14 and which totaled to 4. Coordinates of the two oxygen atoms with populations of 0.7 (O(61)) and 0.5 (O(62)) were refined, but all other parameters for atoms of this group were fixed. R = 0.051, for 2954 reflections with $F_o^2 > 3\sigma(F_o^2)$ in Laue symmetry $2/m$ and 0.058 for 5669 reflections in Laue symmetry 2. R_w on F^2 = 0.012 (in $2/m$) and 0.016 (in 2), S = 1.86 (in $2/m$) and 1.55 (in 2), $(\Delta/\sigma)_{max}$ = 0.14, $(\Delta\rho)_{min}$ = –0.71 e Å^{-3}, and $(\Delta\rho)_{max}$ = 1.39 e Å^{-3} all near Cl(6).

Structural Determination of Λ,*syn*-β-[Rh[(*R,R*)-Me$_2$trien]phi][(+)-Sb-tartrate]$_2$ClO$_4$·8H$_2$O (ent-1f-[(+)-Sb-tartrate]$_2$ClO$_4$·8H$_2$O). A pale yellow triangular prism was obtained from an aqueous solution of **ent-1f**-(ClO$_4$)$_3$ and (+)-KSb-tartrate by slow evaporation at room temperature. A total of 25 reflections with 26° < 2θ < 32° were used to determine the cell dimensions. An empirical absorption correction was applied to the data set. The maximum and minimum relative transmission factors were 1.042 and 0.940. Data were collected from h = –13 to +13, k = –13 to +13 and l = –14 to +14. A total of 9035 reflections were measured to $(\sin\theta)/\lambda$ = 0.59 Å^{-1}; 4141 were independent and were used in the refinement. The goodness of fit for merging (S) was 2.80. Rhodium and antimony atom coordinates were found from the Patterson map, and remaining atoms, by structure factor–Fourier calculation. R = 0.043 on F for 4062 reflections with $F_o^2 > 0$, R = 0.040 on F for 3828 reflections with $F_o^2 > 3\sigma(F_o^2)$. R_w on F^2 = 0.010 for 4141 reflections. S = 3.34 for 4141 reflections and 575 parameters. $(\Delta/\sigma)_{max}$ in the final least-squares cycle was 0.11 for all except O(24). $\Delta\rho_{max}$ = +0.91 e Å^{-3}, $\Delta\rho_{min}$ = –0.59 e Å^{-3}. Secondary extinction parameter was 0.91(11).

Scheme 1



1a-1f

Equilibration Studies. Pure isomers **1a–f** were isolated by HPLC as described above. Each isomer was dissolved in buffer pH 10 (buffer: 0.05 M K$_2$CO$_3$, K$_3$BO$_3$, KOH) for about 3 min and analyzed by HPLC (eluent: CH$_3$CN:H$_2$O:TFA = 13:87:0.1). The ratio of isomers was assumed to be proportional to the ratio of peak areas. As expected, the C_2-symmetric α-isomers **1a** and **1d** were inert to base treatment (pH 10). No isomerization occurred. Treatment of either one, **1b** or **1c** with buffer pH 10 resulted in the same **1b–1c** mixture with a ratio of about 57:43. Treating **1e** or **1f** with pH 10 buffer resulted in a mixture of **1e** and **1f** in a ratio of 27:1. It should be noted that the equilibrium constants between **1b**/**1c** and **1e**/**1f** are pH dependent. However, this behavior was not examined in detail.

Photolysis of Rhodium(III) Complexes and Determination of Quantum Yields. A solution of Λ,α-[Rh[(*S,S*)-Me$_2$trien]phi]Cl$_3$ (**1a**-Cl$_3$) (5 mL, 30 μM) in buffer R (50 mM NaCl, 5 mM Tris, pH 7) was added to a quartz cuvette (l = 2 cm, V = 5 cm^3) containing a small stir bar. If the experiment was performed at pH 10, the complex was dissolved in buffer R and the pH was adjusted by adding NaOH. The cuvette was positioned in the beam of the He/Cd laser and irradiated for time intervals of 10–20 min (at pH 10) or at intervals of several hours (at pH 7) while the solution was stirred vigorously. The electronic absorption spectrum of the solution was recorded after each time interval. Care was taken to obtain an array of readings at short irradiation times where the reaction was less than 30% complete and the plot absorption versus time was linear. The extent of photoreaction with time was quantitated on the basis of absorbance changes at the low-energy maximum near 370 nm. The photoproducts did not absorb to a substantial amount at the monitoring wavelength. In the determination of quantum yields for the photoreaction, only initial irradiation time points were used.

Results and Discussion

Syntheses. As shown in Scheme 1, two strategies for the synthesis of a variety of phenanthrenequinone diimine complexes [Rh(L$_4$)phi]$^{3+}$ have been developed[3] and may be applied here. First the chiral ligands (*S,S*)- and (*R,R*)-2,9-diamino-4,7-diazadecane (Me$_2$trien) are synthesized in three steps from N-protected L- or D-alanine.[8] Very efficient for the assembly of the complex is a one-pot synthesis in which RhCl$_3$ is first reacted with the phi precursor 9,10-diaminophenanthrene and subsequently with the other ancillary ligands L, followed by air oxidation (method A). Using this method for the synthesis of α-[Rh[(*S,S*)-Me$_2$trien]phi]$^{3+}$, we obtained a mixture of isomers in good yield (45%). HPLC analysis however showed that less than 2% of the desired C_2-symmetric α-isomers **1a** and **1d** are formed. Changes of reaction parameters (temperature, pH) did not result in a

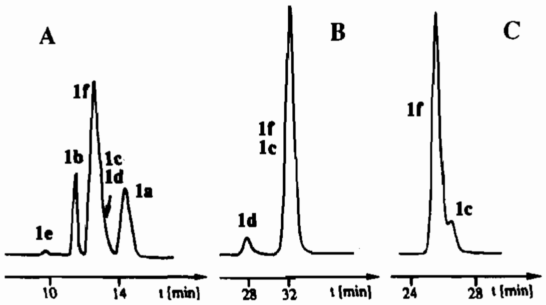


Figure 2. HPL-chromatographic analysis of the isomers [Rh[(*S*,*S*)-Me_2trien]phi]$^{3+}$ on a reversed phase (C_{18}) column, detector wavelength 254 nm: (A) Mixture of six isomers **1a–f** (eluent CH_3CN:H_2O:TFA = 13:87:0.1; *f* = 7.0 mL/min); (B) mixture of **1c**, **1d**, and **1f** (eluent MeOH:H_2O:TFA = 20:80:0.1; *f* = 4.5 mL/min); (C) mixture of **1c** and **1f** (eluent CH_3CN:H_2O:TFA = 11:89:0.1; *f* = 9.0 mL/min).

significant formation of **1a** and **1d**. The ratio of β-isomers **1b** + **1c** with Λ-chirality at the rhodium center to β-isomers **1e** + **1f** with Δ-chirality was 1:1.

In an alternate strategy we first reacted $RhCl_3$ with (*S*,*S*)-Me_2trien·4HCl to give [Rh(*S*,*S*)-Me_2trien)Cl_2]Cl.[9] This complex was hydrolyzed subsequently with aqueous sodium hydroxide and perchloric acid to form the corresponding aquo complex [Rh-(*S*,*S*)-Me_2trien)$(H_2O)_2$]$^{3+}$. Without further isolation or purification this complex was reacted with 9,10-diaminophenanthrene and subsequently oxidized with air to form [Rh[(*S*,*S*)-Me_2trien]-phi]$^{3+}$ (**1**). After cation exchange chromatography, a mixture of diastereomeric complexes **1a–f** was obtained in 50% yield. The ratio of peak areas in the HPLC (λ = 254 nm) **1a**:**1b**:**1c**:**1d**:**1e**:**1f** was 25:13:10:4:1:47. Slight variations of this ratio have been observed in different reactions. This strategy allows one to obtain 30% of the total amount of [Rh[(*S*,*S*)-Me_2trien]phi]$^{3+}$ as the desired C_2-symmetric α-isomers. The ratio **1a**:**1d** is 6:1. The ratio of rhodium complexes containing the Λ-configuration (**1a–c**) to complexes with the Δ-configuration (**1d–f**) is about 1:1, indicating that the chiral tetradentate ligand (*S*,*S*)-Me_2trien did not induce significant asymmetric induction at the Rh center.

The identical synthetic strategy was used for the preparation of [Rh[(*R*,*R*)-Me_2trien]phi]$^{3+}$ (**ent-1a–ent-1f**) with parallel results. The availability of many natural and unnatural amino acids together with the generality of the synthetic scheme opens the possibility of preparing a variety of enantiomerically pure complexes of [Rh(R_2trien)phi]$^{3+}$.

C_{18}-reversed-phase HPLC may be used as a powerful tool to analyze precisely and separate the different isomers with high resolution on an analytical as well as a preparative scale. Representative chromatograms are shown in Figure 2. The six diastereomers were at first resolved into four peaks using isocratic conditions with the solvent system acetonitrile–water–trifluoroacetic acid (TFA) (A). Peaks 1, 2, and 4 were pure isomers according to ^{1}H NMR analysis and were identified as **1e**, **1b**, and **1a** (*vide infra*), respectively. The main peak 3 was resolved into two peaks upon replacing aceonitrile with methanol in the eluent (B). This scheme allowed us to separate **1d** from **1c** and **1f**. Finally, **1c** and **1f** were separated using a slightly more polar eluent of acetonitrile–water–TFA (C).

The identities of **1a–f** were established by a combination of X-ray crystal structure analysis and equilibration studies. In addition, spectroscopic methods in solution (^{1}H NMR, UV, CD) showed characteristic features of each compound, which seem to be general for isomers with the formula [Rh[(*S*,*S*)-R_2trien]phi]$^{3+}$.

Crystallographic Characterization of 1a, 1b, ent-1d, and ent-1f. ^{1}H NMR spectroscopy allows one to distinguish between α, *syn*-β- and *anti*-β-isomers (*vide infra*), but the absolute configuration at the rhodium center (Λ versus Δ) requires further analysis, such as through X-ray crystallography. Since the absolute configuration at the two centers of chirality in the Me_2trien ligand are known from the synthesis, the assignment of the absolute configuration at the Rh may be made unambiguously in the crystal structure analysis. The three-dimensional atom positioning is, furthermore, key to any predictive design of DNA recognition elements. ORTEP drawings of the structures of the cations of Λ,α-[Rh[(*S*,*S*)-Me_2trien]phi]$^{3+}$ (**1a**), Λ, *anti*-β-[Rh-[(*S*,*S*)-Me_2trien]phi]$^{3+}$ (**1b**), Λ,α-[Rh[(*R*,*R*)-Me_2trien]phi]$^{3+}$ (**ent-1d**) and Λ,*syn*-β-[Rh[(*R*,*R*)-Me_2trien]phi]$^{3+}$ (**ent-1f**) with the atomic numbering scheme are displayed in Figures 3–6, respectively. The crystals of Λ,α-[Rh[(*S*,*S*)-Me_2trien]phi]Cl-$(PF_6)_2$·$2H_2O$(**1a**-Cl$(PF_6)_2$·$2H_2O$), Λ,*anti*-β-[Rh[(*S*,*S*)-Me_2trien]-phi]Cl_3·3.9 H_2O (**1b**-Cl_3·3.9H_2O), Λ,α-[Rh[(*R*,*R*)-Me_2trien]-phi]$(ClO_4)_3$ (**ent-1d**-$(ClO_4)_3$) and Λ,*syn*-β-[Rh[(*R*,*R*)-Me_2trien]-phi][(+)-Sb-tartrate]$_2$$ClO_4$·$8H_2O$ (**ent-1f**-[(+)-Sb-tartrate]$_2$-ClO_4·$8H_2O$) consist of monomeric cations, the corresponding counterions, and lattice water molecules. Selected bond lengths and angles are given in Table 2. Torsion angles were obtained from MacroModel and are given in Table 3. Final heavy atom parameters, assigned hydrogen atom parameters, anisotropic displacement parameters, and complete distances and angles are provided as supplementary material.

The Rh atom in all four complexes is in a slightly distorted octahedral coordination geometry with the metal center being coordinated by two primary and two secondary amines from the tetradentate Me_2trien ligand and two imine nitrogen atoms from the phi ligand. The Rh–NH_2R and Rh–NHR_2 distances average 2.06 Å, with actual values between 2.021 and 2.086 Å and are in line with those found for similar Rh–amine complexes.[3] Rh–imine bond lengths are slightly shorter, averaging to 2.02 Å, with actual values ranging from 1.997(4) to 2.041(3) Å. In **1a**, **ent-1d**, and **ent-1f** both Rh–imine bond lengths are identical; however,

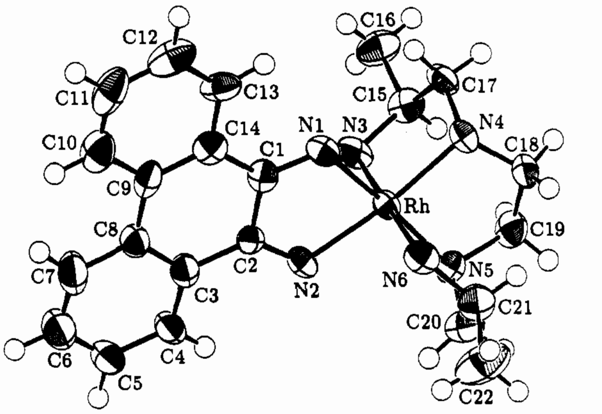


Figure 3. ORTEP drawing of Λ,α-[Rh[(*S*,*S*)-Me_2trien]phi]$^{3+}$ (**1a**) with the numbering system used. Heavy atoms are shown as 50% ellipsoids; hydrogen atoms are shown as arbitrary, small spheres.

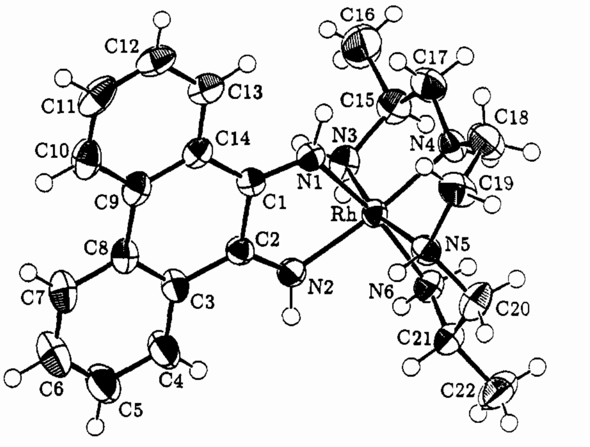


Figure 4. ORTEP drawing of Λ,*anti*-β-[Rh[(*S*,*S*)-Me_2trien]phi]$^{3+}$ (**1b**) with the numbering system used. Heavy atoms are shown as 50% ellipsoids; hydrogen atoms are shown as arbitrary, small spheres.

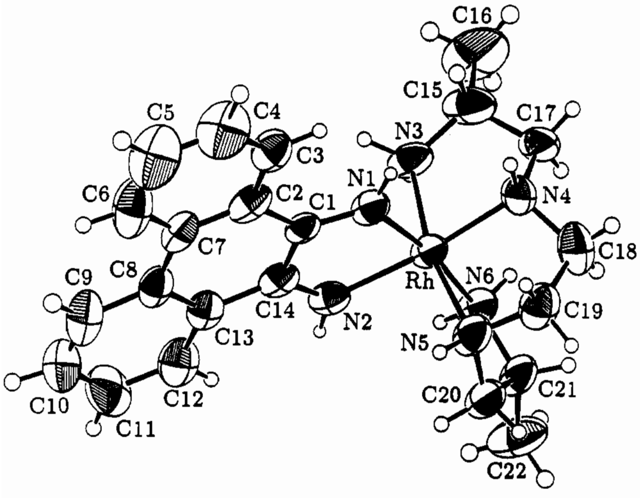


Figure 5. ORTEP drawing of Λ,α-[Rh[(*R*,*R*)-Me_2trien]phi]$^{3+}$ (**ent-1d**) with the numbering system used. Heavy atoms are shown as 70% ellipsoids; hydrogen atoms are shown as arbitrary, small spheres.

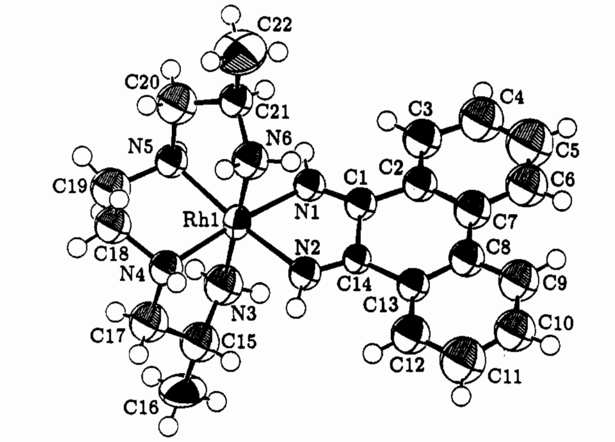


Figure 6. ORTEP drawing of Λ,*syn*-β-[Rh[(*R*,*R*)-Me_2trien]phi]$^{3+}$ (**ent-1f**) with the numbering system used. Heavy atoms are shown as 50% ellipsoids; hydrogen atoms are shown with thermal parameters 0.1 times those assigned.

in **1b** the Rh–N(1)$_{imine}$ distance cis to the secondary amine N(4) is 2.041(3) Å compared to 1.997(4) Å for the Rh–N(2)$_{imine}$ distance cis to the primary amine N(6). Deviations from ideal octahedral geometry are seen in the N–Rh–N angles. The small N(1)–Rh–N(2) angles average 77.5°, which is due to the inherently small bite of the phi ligand. The bite angles N–Rh–N of the tetradentate ligand Me_2trien are very similar in all four complexes and average 83.2° with actual values between 81.0 and 85.2°. The differences in strain between α- and β-isomers are apparent in the angles between the two axial coordinated nitrogens. The N(3)–Rh–N(6) angle in the C_2-symmetric complexes **1a** and **ent-1d** is close to octahedral geometry (178.3, 178.8°). The corresponding angle in β-isomers **1b** and **ent-1f**, N(3)–Rh–N(5), shows a considerable distorsion from ideal octahedral geometry (166.1, 166.6°), which is intermediate between the angle observed in the α-isomers **1a** and **1d** and that observed [Rh([12]aneN_4)phi]$^{3+}$ (N_{ax}–Rh–N_{ax} = 160°),[3] a complex with four fused five-membered rings. The CH_3 groups in all structures occupy equatorial positions. Therefore the chirality at the CH_3 group determines the chiral conformation of the chelate ring. Chiral chelate rings with *S*-configuration at the CH_3 group are puckered in δ-conformations. The chiral conformations are δ, λ, δ in **1a**, δ, δ, δ in **1b**, λ, λ, λ in **ent-1d**, and λ, δ, λ in **ent-1f**. Torsion angles are given in Table 3.

Table 2. Selected Bond Lengths and Angles in Phi Complexes of Rh(III)

	1a	**1b**	**ent-1d**	**ent-1f**
		Distance (Å)		
Rh–N(1)	2.032(8)	2.041(3)	1.996(15)	2.003(12)
Rh–N(2)	2.028(8)	1.997(4)	2.013(15)	2.021(11)
Rh–N(3)	2.086(8)	2.076(5)	2.047(17)	2.063(13)
Rh–N(4)	2.081(8)	2.038(4)	2.046(15)	2.021(13)
Rh–N(5)	2.059(8)	2.049(4)	2.064(14)	2.049(13)
Rh–N(6)	2.079(8)	2.064(4)	2.064(16)	2.059(12)
N(1)–C(1)	1.310(12)	1.291(5)	1.26(2)	1.290(17)
N(2)–C(2)	1.294(14)	1.271(6)	1.24(2)[a]	1.309(17)[a]
		Angle (deg)		
N(1)–Rh–N(2)	77.8(3)	77.2(2)	77.2(6)	77.7(5)
N(1)–Rh–N(3)	89.8(3)	91.1(2)	94.7(6)	91.3(5)
N(1)–Rh–N(4)	98.2(3)	97.2(1)	174.5(6)	92.4(5)
N(1)–Rh–N(5)	174.5(3)	93.4(1)	101.2(6)	95.3(5)
N(1)–Rh–N(6)	91.7(3)	169.1(1)	86.2(6)	171.5(5)
N(2)–Rh–N(3)	89.9(3)	94.8(2)	89.3(6)	96.9(5)
N(2)–Rh–N(4)	172.3(3)	174.2(2)	99.2(6)	170.1(5)
N(2)–Rh–N(5)	100.1(3)	99.1(2)	172.5(6)	95.9(5)
N(2)–Rh–N(6)	91.3(3)	93.0(2)	90.2(6)	94.3(5)
N(3)–Rh–N(4)	83.5(3)	84.0(2)	81.0(6)	82.8(5)
N(3)–Rh–N(5)	95.3(3)	166.1(2)	98.2(6)	166.6(5)
N(3)–Rh–N(6)	178.3(3)	94.5(2)	178.8(7)	92.4(5)
N(4)–Rh–N(5)	84.5(3)	82.3(2)	83.0(6)	85.2(5)
N(4)–Rh–N(6)	95.4(3)	92.7(2)	98.0(6)	95.6(5)
N(5)–Rh–N(6)	83.2(3)	83.4(2)	82.4(6)	82.7(5)

[a] Bond length N(2)–C(14).

Table 3. Torsion Angles (deg) of Phi Complexes of Rh(III)

	1a	**ent-1d**	**1b**	**ent-1f**
N(3)–C(15)–C(17)–N(4)	50.9	–46.0	50.0	–48.8
C(15)–C(17)–N(4)–C(18)	80.1	142.3	–178.3	170.0
C(17)–N(4)–C(18)–C(19)	–90.9	–81.4	129.2	–166.3
N(4)–C(18)–C(19)–N(5)	–38.8	–52.4	26.9	48.1
C(18)–C(19)–N(5)–C(20)	–94.9	–82.0	77.7	88.4
C(19)–N(5)–C(20)–C(21)	80.5	138.8	–151.2	–75.6
N(5)–C(20)–C(21)–N(6)	50.1	–45.7	53.4	–44.2

Chemical Correlation between β-Isomers. Under basic conditions rapid equilibration between **1b** and **1c** as well as between **1e** and **1f** occurs. The thermodynamic equilibrium, which appeared to be pH-dependent, was investigated at pH 10. Treatment of either **1b** or **1c** with pH 10 buffer results in rapid formation of a mixture of the two complexes in thermodynamic equilibrium in a ratio of 57:43 (according to HPLC analysis) due to epimerization of the secondary amine at the equatorial coordination site. This equilibration indicates that, in the case of the (2*S*,9*S*)-Me_2trien ligand, the conformational constraints and interligand interactions upon changing the configuration at the equatorial nitrogen for rhodium complexes with the Λ-configuration are very similar. At pH 10 the *anti*-β-isomer **1b** is only about 0.69 kJ mol^{-1} more stable than the *syn*-β-isomer **1c** at room temperature. The ratio of **1e** to **1f** with the Δ-configuration in thermodynamic equilibrium at pH 10 is 1:27, favoring the *syn*-β-isomer **1f** by a ΔG of 8.0 kJ mol^{-1}. In acidic solutions (pH <2.5) no epimerization of β-isomers was observed, indicating that under these conditions the necessary conformational reorganization of the chelate rings is slower than the inversion at the equatorial amines. The C_2-symmetric α-isomers do not possess configurational flexibility at the chiral secondary amines; the configuration is determined by the absolute configuration of the rhodium, and therefore, under the same conditions (pH 10), no base-catalyzed isomerization is observed.

Two α-isomers (**1a**, **ent-1d**) and two β-isomers, one with a syn (**ent-1f**) and one with an anti configuration (**1b**) have been characterized in the solid state. Since **ent-1d** and **ent-1f** are the enantiomers of **1d** and **1f** and since thermodynamic equilibria exist between **1b**/**1c** and **1e**/**1f**, the absolute and relative structures of all six diastereomers [Rh(*S*,*S*)-Me_2trien)phi]$^{3+}$ have been assigned.

Spectroscopic Characterization. Given the absolute and relative structures of the complexes **1a**–**f** from the crystallographic studies and the equilibration studies, we may characterize the rhodium

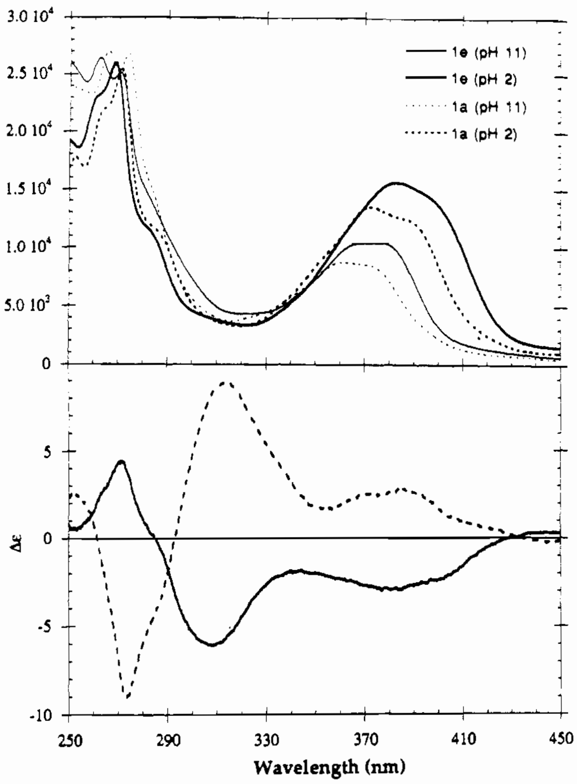


Figure 7. Top: UV spectra of Λ,α-[Rh[(*S,S*)-Me$_2$trien]phi]$^{3+}$ (**1a**) (···) and Δ,*cis*-β-[Rh[(*S,S*)-Me$_2$trien]phi]$^{3+}$ (**1f**) (—) at pH 2 (bold) and pH 11 (standard). Bottom: CD spectra of Λ,α-[Rh[(*S,S*)-Me$_2$trien]phi]$^{3+}$ (**1a**) (···) and Δ,*cis*-β-[Rh[(*S,S*)-Me$_2$trien]phi]$^{3+}$ (**1f**) (—).

complexes in solution by ^{1}H NMR, UV, and CD spectroscopy in that context. The ^{1}H NMR spectra show features which may be used for the general assignment of the coordination geometry adopted by this tetradentate ligand. α- and β-isomers of **1** can easily be distinguished on the basis of symmetry considerations; α-isomers **1a** and **1d** display C_2-symmetry while β-isomers **1b**, **1c**, **1e**, and **1f** display C_1-symmetry. This symmetry difference results for α-isomers in one doublet for the two methyl groups at 1.0–1.1 ppm and a symmetric pattern for the aromatic protons of the phi ligand, compared, for β-isomers, to two doublets at 1.1–1.4 ppm for the two magnetically nonequivalent methyl groups and a nonsymmetric splitting pattern for the aromatic protons of the phi ligand. Moreover, ^{1}H NMR allows one to distinguish β-isomers with an anti configuration at the equatorial secondary amine (**1b** and **1e**) from β-isomers with a syn configuration (**1c** and **1f**). An anti configuration at the equatorial donor atom results in a downfield shift of one of the aromatic protons of the phi ligand from 8.2 to 8.5 ppm. As seen in other phi complexes of Rh(III),[3] this difference in chemical shifts in the aromatic ligand provides a sensitive indicator of the relative configurations at heteroatoms coordinated in the equatorial plane.

Complexes **1a–f** have the characteristic electronic absorption spectra of rhodium complexes containing the phenanthrenequinone diimine ligand.[2,3] Spectral features include strong absorption bands between 250 and 280 nm (ϵ = 18 000–26 000 M^{-1} cm^{-1}) and a broad band around 380 nm. The wavelengths of the low-energy maximum as well as the shapes differ for the α- and β-isomers. Representative spectra of the Λ,α-isomer **1a** and the Δ,β-isomer **1f** (contains about 4% **1e**) at pH 2 and at pH 11 are shown in Figure 7. At pH 7, the maximum of α-isomers **1a** and **1d** is found at 373 nm with a shoulder at 386 nm, whereas in β-isomers the maximum is red-shifted to 386 nm. The energy of this transition has been correlated with the coordination geometry of the ancillary ligands. The larger the distortion from octahedral geometry, seen in the angle N$_{ax}$–Rh–N$_{ax}$, (178.3, 178.8° in α-isomers; 166.1, 166.6° in β-isomers), the more red-shifted is the low-energy transition, indicating some mixing between the metal-centered d-orbitals and the π-system of the phi ligand.[3] As seen in other phi complexes of rhodium(III), spectral changes are observed upon changing the pH from pH 2 to pH 11 due to deprotonation at the imine groups of the phi ligand. When the pH is changed from pH 7 to pH 11, the maximum of **1a** shifts from 373 nm (ϵ = 13 500 M^{-1} cm^{-1}) to 362 nm (ϵ = 8800 M^{-1} cm^{-1}) with a shoulder at 372 nm (ϵ = 8600 M^{-1} cm^{-1}). The maximum of the β-isomer **1f** (containing about 4% **1e**) shifts from 386 nm (ϵ = 15 500 M^{-1} cm^{-1}) to a broad band at 372–381 nm (ϵ = 10 400 M^{-1} cm^{-1}). It is also observed that the peak area is reduced substantially. These spectral changes are completely reversible over the pH range pH 2–11. Plotting the absorbance at the low-energy maximum versus pH yields a curve with an inflection point at pH 9.1 for **1a** and at pH 8.9 for **1f**, an indicator of one of the pK_a's of the coordinated phi's in these complexes.[2]

The CD spectra reflect the absolute configuration of the rhodium. CD spectra of the Λ,α-isomer **1a** and the Δ,*cis*-β-isomer **1f** are also shown in Figure 7. Λ-Enantiomers (α and β-geometry) show a positive Cotton effect and Δ-enantiomers show a negative Cotton effect near 290 nm.

As with other phi complexes of rhodium(III),[3] irradiation of an aqueous solution of **1a** with UV light (λ = 325 nm) leads to degradation of the complex with the loss of the phi ligand as evident from the UV spectra. The quantum yield for photoanation is significantly higher at a pH above the pK_a of the complex. The quantum yield for photoanation of **1a** is 10×10^{-4} mol/einstein at pH 10 compared to 0.5×10^{-4} mol/einstein at pH 7.

Comparative Studies with Other Isomeric Mixtures. The present study represents a full structural characterization of a family of coordination isomers. A considerable body of work has also been carried out with respect to the preparation and structural elucidation of trien complexes of cobalt(III) with different achiral and chiral ligands,[13] and it is interesting to explore any parallels with the present work. The aquation of [Co(trien)Cl$_2$]$^+$ is characterized by the retention of absolute configuration in the case of *cis*-α and *cis*-β complexes, but complete isomerization of the *trans*-isomer to the *cis*-β-isomer, indicating the higher thermodynamic stability of the cis complexes. The relative thermodynamic stability of the α- and β-isomers for [Co(trien)X$_2$]$^+$ varies as a function of the substituent X, favoring the α-isomer if X = Cl or NO$_2$ and favoring the β-isomer if X = H$_2$O or an amino acid anion. Thus relative isomer stabilities for the diaquo and amino acid complexes resemble those found with [Rh[Me$_2$trien]phi]$^{3+}$. Interestingly, the kinetics of isomerization at the chiral nitrogen in the equatorial position of the Λ-*syn*-β-[Co(trien)(H$_2$O)$_2$]$^{3+}$ to the thermodynamically more stable Λ-*anti*-β-isomer has also been investigated.[14] The complete isomerization of the *syn*-β- to the *anti*-β-isomer is consistent with the calculated difference of the conformational energy of the two epimers of 3.0 kcal/mol. In a whole range of trien complexes of cobalt, the anti-configuration at the chiral nitrogen in the equatorial plane appears to be the more stable configuration.[15] In our case, we find the syn conformation overall to be favored (% anti = **1b** + **1e** = 14% versus % syn = **1c** + **1f** = 57%). But this difference is not surprising, since for these complexes there are two determining factors: (i) the intrinsic conformational requirements of the trien ligand; also (ii) the preference of the methyl group for occupation of an equatorial position in the five-member chelate ring. This factor then affects the configuration

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[13] (a) Sargeson, A. M.; Searle, G. H. *Nature*, **1963**, *200*, 365. (b) Sargeson, A. M.; Searle, G. H. *Inorg. Chem.* **1967**, *6*, 787. (c) Marzilli, L. G.; Buckingham, D. A. *Inorg. Chem.* **1967**, *6*, 1042.

[14] Buckingham, D. A.; Marzilli, P. A.; Sargeson, A. M. *Inorg. Chem.* **1967**, *6*, 1032.

[15] Buckingham, D. A.; Sargeson, A. M. *Top. Stereochem.* **1971**, *6*, 219.

[16] (a) Asperger, R. G.; Liu, C. F. *Inorg Chem.* **1965**, *4*, 1395. (b) Asperger, R. G. Dissertation, University of Michigan, 1965. (c) Asperger, R. G. *Inorg. Chem.* **1969**, *8*, 2127.

of the chiral nitrogen. Thus we find, for the Λ-isomers, it is the anti epimer which is favored (anti/syn = 57/43) whereas for the Δ-isomers, syn is preferred (anti/syn = 1/27). Perhaps more intriguing, the same absolute configuration about the rhodium is found to be favored in the preparation of *cis*-α-[Co(Me$_2$trien)-Cl$_2$]$^+$, where the ratio of isolated material was found to be 95:4 (Λ:Δ).[16] These comparisons with studies of cobalt complexes, then, reveal some interesting parallels. However, both in this system and in past studies, any general predictions of favored isomeric products is difficult, at best, owing to the sensitivity of product mixtures to experimental conditions.

Conclusion. The preparation, separation and detailed crystallographic and spectroscopic characterization of the six diastereomers [Rh[(*S*,*S*)-Me$_2$trien]phi]$^{3+}$ have been carried out. These studies point to the general thermodynamic stability of the *cis*-β configuration, compared to the C_2-symmetric α-configuration, although the relative proportions of isomers formed, as with other coordination complexes, is a sensitive function of the conditions of preparation. This structural series now provides a stereochemically well-defined framework for the systematic study of DNA recognition by metallointercalators. On the basis of the data presented, a combination of ^{1}H NMR and CD spectroscopy should be sufficient for the assignment of absolute and relative configurations in the complexes [Rh(R$_2$trien)phi]$^{3+}$.

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Supplementary Material Available: Tables of final heavy atom parameters, assigned hydrogen atom parameters, anisotropic displacement parameters and complete distances and angles for Λ,α-[Rh[(2*S*,9*S*)-Me$_2$trien]phi](PF$_6$)$_2$Cl·2H$_2$O, Λ,*anti*-β-[Rh[(2*S*,9*S*)-Me$_2$trien]phi]Cl$_3$·3.9H$_2$O, Λ,α-[Rh[(2*R*,9*R*)-Me$_2$trien]phi](ClO$_4$)$_3$, and Λ,*syn*-β-[Rh-[(2*R*,9*R*)-Me$_2$trien]phi][(+)-Sb-tartrate]$_2$ClO$_4$·8H$_2$O (45 pages). Ordering information is given on any current masthead page.