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Efficient Enantioselective Extraction of Tris(diimine)ruthenium(II) Complexes by Chiral Lipophilic TRISPHAT Anions.

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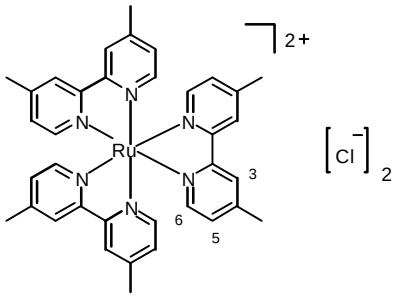
General Information. All reactions were carried out under an atmosphere of dry nitrogen using Schlenk lines techniques with magnetic stirring, unless otherwise stated. Solvents were dried and distilled prior to use. Chloroform (Fluka) and $CDCl_3$ were filtered on basic alumina before use. Deionized water was used. Analytical thin layer chromatography was performed on Macherey-Nagel 0.25 mm silica gel plates. Visualization was accomplished with UV light. ^1H, ^{13}C and ^{31}P NMR spectra were recorded on Varian XL-200 (200 MHz) and Bruker AMX-400 (400 MHz) spectrometers. Chemical shifts are given in ppm. ^1H and ^{13}C chemical shifts were reported relative to Me_4Si, δ and J values correspond to the common 'first order analysis' of the spectra, multiplicity were determined by Dept 135° (C_q: quaternary carbon). Data are reported as: (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constant(s) in Hz; integration; proton assignments). ^{31}P chemical shifts were reported relative to H_3PO_4. Infrared spectra were recorded on a Perkin-Elmer 1600 FT-IR spectrophotometer by using NaCl cells or KBr disks. The absorption is indicated in wave numbers (cm^{-1}) and the intensities are represented as strong (s), medium (m) and weak (w). Optical rotations were determined on a Perkin Elmer 241 polarimeter in a thermostated (20°C) 10 cm long microcell with sodium or mercury lamps and are reported as follows: $[\alpha]^{20}_{\lambda}$ (c g/100 mL, solvent). UV spectra were recorded on a UVIKON 860 spectrometer in a 1 cm quartz cell; λ_{max} were given in nm and molar adsorption coefficient ε in $mol^{-1}.L.cm^{-1}$. Circular dichroism spectra were recorded on a JASCO J-715 spectropolarimeter in a 1 cm quartz cell; λ were given in nm and molar circular-dichroic absorption $\Delta\varepsilon$ in $mol^{-1}.L.cm^{-1}$. Electronspray mass spectra were obtained on a Finnigan SSQ 7000 spectrometer. Melting points (M.p.) were determined on a Stuart Scientific SMP3 melting point apparatus and are uncorrected. When a mixture of diastereomers is present, ^1H NMR data for the major and *minor* isomers will be presented in regular and *italic* formats respectively.

General Procedure for the preparation of racemic $[Ru(LL)_3][PF_6]_2$ salts :

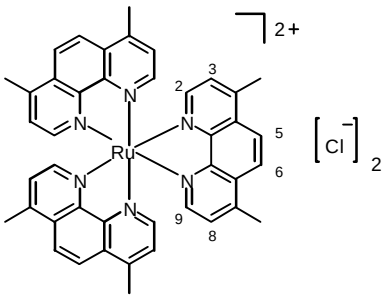
In a 2-neck flask (25 mL) equipped with a condenser and a magnetic stirrer, a suspension of 261 mg (540 μmol, 1.0 equiv.) of $Ru(DMSO)_4Cl_2$ and 3.0 equiv. of bipyridine or phenanthroline ligands in ethylene glycol (10% water, 10 mL) was heated at 120°C for 1 hour under a nitrogen atmosphere (TLC monitoring). The resulting orange colored solution was cooled to 20°C, diluted with water (30 mL), and to which was added a saturated solution of ammonium hexafluorophosphate salt until all coloured material has precipitated. The solid was filtered, dissolved in the minimum amount of CH_2Cl_2 and precipitated again with ether. After filtration and drying *in vacuo*, the titled compounds are afforded in decent to good yields and no need of further purification is required.

$[Ru(diimine)_3]Cl_2$ salts :



$[Ru(4,4'\text{-dimethyl-}2,2'\text{-bipyridine})_3]Cl_2$ or $[4]Cl_2$. 900 mg of Dowex 1X were added to a suspension of 472 mg (0.50 mmol) of $[Ru(4,4'\text{-dimethyl-}2,2'\text{-bipyridine})_3][PF_6]_2$ salt in water (25 mL). The mixture was heated to reflux until complete solubilization of the orange salt. After filtration over a hot funnel, washing with hot water and concentration *in vacuo*, 362 mg of dichloride salt were obtained (99% yield) as a red-orange solid.

M.p. > 250°C (decomp.). **^1H NMR** (400 MHz, 20% $[D_6]$DMSO in $CDCl_3$): 8.29 (s, 6H, H(3)); 7.07 (d, ^3J=6.0 Hz, 6H, H(6)); 6.90 (d, ^3J=5.6 Hz, 6H, H(5)); 2.21 (s, 18H, H(Me)). **^{13}C NMR** (100 MHz, 20% $[D_6]$DMSO in $CDCl_3$): 156.3 (C, 6C); 150.1 (CH, 6C, C(5)); 149.7 (C, 6C); 128.5 (CH, 6C, C(6)); 125.4 (CH, 6C, C(3)); 21.1 (CH_3, 6C, C(Me)). **IR** (KBr): 3401 (m), 3011 (m); 1618 (m); 1478 (m); 1446 (m); 1304 (w); 1240 (w); 1039 (w); 832.7 (m). **ES-MS**: (+) 326.4 $[C_{36}H_{36}N_6Ru]^{2+}$.

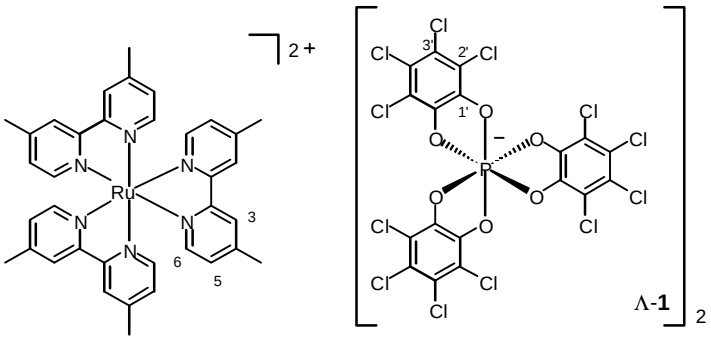


[Ru(4,7-dimethyl-1,10-phenanthroline)$_3$]Cl$_2$ salt or [5]Cl$_2$. 60 mg of Dowex 1X were added to a suspension of 51 mg (0.050 mmol) of [Ru(4,7-dimethyl-1,10-phenanthroline)$_3$][PF$_6$]$_2$ salt in water (5 mL). The mixture was heated at reflux for one hour. After filtration over a hot funnel, washing with hot water and evaporation, 39.1 mg of dichloride salt were obtained (0.049 mmol, 98% yield) as a red-orange solid.
M.p. > 330°C (decomp.). **^{1}H NMR** (400 MHz, 20% [D$_6$]DMSO in CDCl$_3$): 8.12 (s, 6H, H(5,6)); 7.61 (d, ^{3}J=5.2 Hz, 6H, H(2,9)); 7.36 (d, ^{3}J=5.6 Hz, 6H, H(3,8)); 2.70 (s, 18H, H(Me)). **^{13}C NMR** (100 MHz, 20% [D$_6$]DMSO in CDCl$_3$): 151.3 (CH, 6C, C(2,9)); 147.3 (C, 6C); 146.8 (C, 6C); 130.5 (C, 6C); 127.0 (CH, 6C, C(3,8)); 124.5 (CH, 6C, C(5,6)); 18.7 (CH$_3$, 6C, C(Me)). **IR** (KBr): 3402 (m); 1624 (m); 1602 (m); 1572 (m); 1516 (w); 1450 (m); 1418 (s); 1227 (w); 1169 (w); 1028 (w); 850 (m); 725 (w). **ES-MS**: (+) 363.0 [$C_{42}H_{36}N_6Ru$]$^{2+}$; 724.6 [$C_{42}H_{36}N_6Ru$]$^+$.

General Procedure for the Asymmetric Extraction of Ru(II)tris(diimine) complexes : In a one-neck round-bottomed flask (25 mL) equipped with a magnetic stirrer, a solution of ruthenium(II)tris(diimine) dichloride salt (0.010 mmol, 1.0 eq.) in 10 mL of water was carefully added to a solution of TRISPHAT salt (0.010 mmol, 1.0 eq.) in 10 mL of $CHCl_3$ ([**2**][Λ-**1**]) or 7.5-10% DMSO in $CHCl_3$ ([**3**][Δ-**1**]).* A partial transfer of orange coloration occurred immediately from the aqueous to the organic layers upon strong stirring of the mixture. After 10 min., the reaction mixture was left standing (5 min.) to insure the complete separation of the organic and aqueous phases. The two phases were separated and the organic layer was washed with water. The organic layer was dried (Na_2SO_4), filtered and concentrated *in vacuo* to afford an orange solid. The diastereomeric purity of the extracted adducts was measured by ^{1}H NMR analysis.[1] The aqueous layer was concentrated *in vacuo* and dried at 50°C for 12h to afford an orange powder. In the experiments performed with [**2**][Λ-**1**], the enantiomeric purity of the [**4**-**5**]Cl$_2$ complexes remaining in the aqueous phases was determined by ^{1}H NMR analysis after addition of 2-3 equiv. of [**2**][Λ-**1**] as NMR chiral shift reagent.[2]

Extraction of [4]Cl$_2$ by [*n*Bu$_3$NH][Λ-1] :
Experiment performed according to the above-described procedure using 9.55 mg (0.010 mmol) of [*n*Bu$_3$NH][Λ-**1**] salt in $CHCl_3$ and 7.25 mg of [**4**]Cl$_2$ in water. Salt [**4**][Λ-**1**]$_2$ is extracted into the organic layer and obtained as an orange-solid (10.5 mg, 46%). From the aqueous layer, 15.2 mg of an orange residue is obtained.

Organic layer:



[Ru(4,4'-dimethyl-2,2'-bipyridine)$_3$](Λ-1)$_2$ salts or [4][Λ-1]$_2$.
^{31}P NMR (162 MHz, 20% [D$_6$]DMSO in CDCl$_3$): -80.1. **^{1}H NMR** (400 MHz, 20% [D$_6$]DMSO in CDCl$_3$, d.r. 8.7:1, ratio of major and *minor* diastereoisomers): *8.15 (s, 6H, H(3))*; 8.08 (s, 6H, H(3)); 7.33 (d, ^{3}J=5.9 Hz, 6H, H(6)); *7.09 (d, ^{3}J=5.9 Hz, 6H, H(6))*; *6.86 (d, ^{3}J=5.5 Hz, 6H, H(5))*; 6.72 (d, ^{3}J=5.5 Hz, 6H, H(5)); *2.20 (s, 18H, H(Me));* 2.09 (s, 18H, H(Me)). **CD** (1% DMSO in CH_2Cl_2, 2.48·10^{-6} M, 20°C): λ(Δε) 295.5 (93); 279.0 (+86); 242.5 (126). **ES-MS**: (+) 327.0 [$C_{36}H_{36}N_6Ru$]$^{2+}$; 1422.7 [$C_{36}H_{36}N_6Ru$][TRISPHAT]$^+$; (-) 768.6 [TRISPHAT]$^-$.

Aqueous layer: **^{1}H NMR** (400 MHz, 20% [D$_6$]DMSO in CDCl$_3$, with addition of 2.7 equiv. of [*n*Bu$_3$NH][Λ-**1**] as chiral shift reagent): for proton H(2,9), Δδ=0.200 ppm, e.r. 8.4:1.

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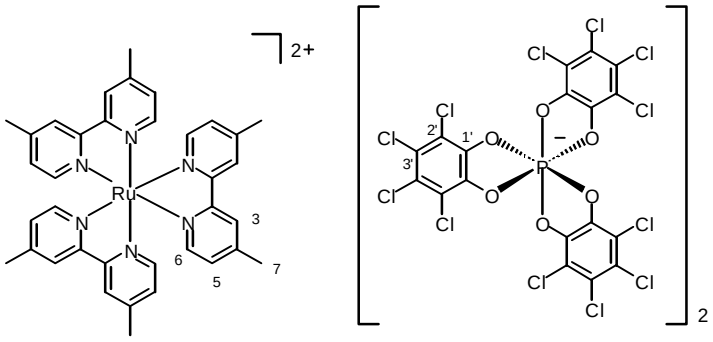
* The solutions of [**3**][Δ-**1**] are prepared by dissolution of the salt in DMSO and then dilution with $CHCl_3$.

Extraction of [4]Cl_2 by [cinchonidinium][Δ-1] :

Experiment performed according to the above-described procedure using 10.6 mg (0.010 mmol) of [cinchonidinium][Δ-**1**] salt in 7.5% DMSO in $CHCl_3$ and 7.25 mg of [**4**]Cl_2 in water. Salt [**4**][Δ-**1**]$_2$ is extracted into the organic layer and obtained as an orange solid (10.0 mg, 46%). From the aqueous layer, 7.5 mg of an orange residue is obtained.

Organic layer:



[Ru(4,4'-dimethyl-2,2'-bipyridine)$_3$][Δ-1]$_2$ salts or [4][Δ-1]$_2$:

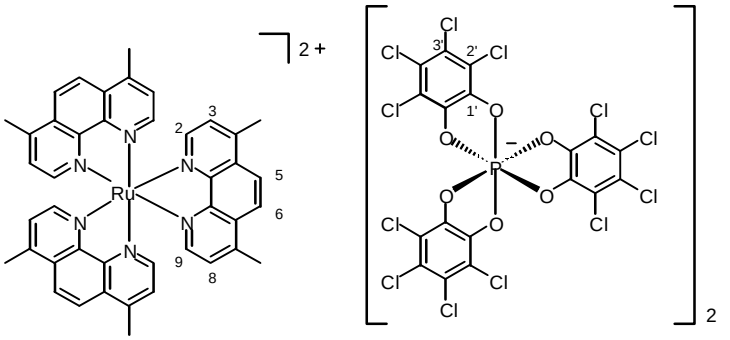
M.p. > 240 °C (decomp.). **^{31}P NMR** (162 MHz, 20% [D_6]DMSO in $CDCl_3$): -80.1. **^{1}H NMR** (400 MHz, 20% [D_6]DMSO in $CDCl_3$, d.r. 12.3:1, ratio of major and *minor* diastereoisomers): *8.09 (s, 6H, H(3))*; 8.03 (s, 6H, H(3)); 7.47 (d, ^{3}J=5.9 Hz, 6H, H(6)); *7.08 (d, ^{3}J=5.9 Hz, 6H, H(6))*; *6.89 (d, ^{3}J=5.5 Hz, 6H, H(5))*; 6.61 (d, ^{3}J=5.5 Hz, 6H, H(5)); *2.20 (s, 18H, H(Me));* 2.06 (s, 18H, H(Me)). **^{13}C NMR** (100 MHz, 80% [D_6]DMSO in $CDCl_3$):† 156.1 (CH, 6C); 149.8 (C, 6C); 149.1 (C, 6C); 141.1 (C, $^2J_{(C\text{-}P)}$=7 Hz, 6C, C(1')); 128.0 (CH, 6C); 124.8 (CH, 6C); 121.8 (C, 6C, C(3')); 113.0 (C, $^3J_{(C\text{-}P)}$=17 Hz, 6C, C(2')); 20.5 (CH_3, 6C, C(Me)). **IR** (CH_2Cl_2): 3052 (m); 2985 (w); 1616 (w); 1273 (s); 1055 (s); 1033 (m); 1011 (m); 815 (w). **UV/Vis** (EtOH, $4.22\cdot10^{-6}$ M): λ_{max} (ε) 664.0 ($1.40\cdot10^4$); 283.0 ($2.24\cdot10^5$); 228.0 ($2.76\cdot10^5$). **CD** (1% DMSO in CH_2Cl_2, $4.22\cdot10^{-6}$ M, 20°C): λ (Δε) 241.0 (-118); 279.0 (85); 294.5 (-153); 483.0 (-9). **ES-MS**: (+) 327.0 $[C_{36}H_{36}N_6Ru]^{2+}$; 1422.7 $[C_{36}H_{36}N_6Ru][TRISPHAT]^+$; (-) 768.6 $[TRISPHAT]^-$.

The major homochiral diastereomer [**Δ-4**][**Δ-1**] can be separated from the *minor* heterochiral [**Λ-4**][**Δ-1**] by flash chromatography over silica gel (eluent CH_2Cl_2):[1] $[\alpha]^{20}_{578}$= -860 (c = 0.011,CH_2Cl_2); **CD** (CH_2Cl_2, $5.2\cdot10^{-6}$ M, 20°C): λ (Δε) 280 (149); 295 (-280); 482 (-17).

Extraction of [5]Cl_2 by [*n*Bu_3NH][Λ-1] :

Experiment performed according to the above-described procedure using 9.55 mg (0.010 mmol) of [*n*Bu_3NH][Λ-**1**] salt in $CHCl_3$ and 8.0 mg of [**5**]Cl_2 in water. Salt [**5**][Λ-**1**]$_2$ is extracted into the organic layer and obtained as an orange-solid (10.2 mg, 45%). From the aqueous layer, 5.3 mg of an orange residue is obtained.

Organic layer:



[Ru(4,7-dimethyl-1,10-phenanthroline)$_3$][Λ-1]$_2$ salt or [5][Λ-1]$_2$.

^{31}P NMR (162 MHz, 20% [D_6]DMSO in $CDCl_3$): -80.1. **^{1}H NMR** (400 MHz, 20% [D_6]DMSO in $CDCl_3$, d.r. > 49:1, only one diastereoisomer is observed): 8.07 (d, ^{3}J=5.2 Hz, 6H, H(2,9)); 7.95 (s, 6H, H(5,6)); 6.81 (d, ^{3}J=5.2 Hz, 6H, H(3,8)); 2.32 (s, 18H, H(Me)). **CD** (1% DMSO in CH_2Cl_2, $4.51\cdot10^{-6}$ M, 20°C): λ(Δε) 261.0 (-136); 270.0 (126); 288.0 (-11). **ES-MS**: (+) 363.1 $[C_{42}H_{36}N_6Ru]^{2+}$; 1494.5 $[C_{42}H_{36}N_6Ru][TRISPHAT]^+$; (-) 768.6 $[TRISPHAT]^-$.

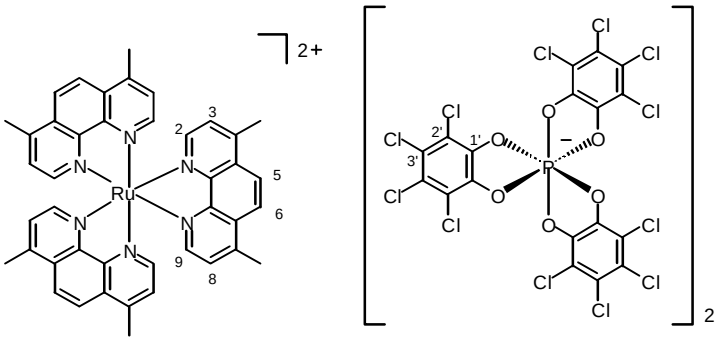
Aqueous layer: **^{1}H NMR** (400 MHz, 20% [D_6]DMSO in $CDCl_3$, with addition of 2.1 equiv. of [*n*Bu_3NH][Λ-**1**] as chiral shift reagent): for proton H(2,9), Δδ=0.063 ppm, e.r. 35:1.

† In this polar solvent mixture, the diastereomers are isochronous.

Extraction of [5]Cl_2 by [cinchonidinium][Δ-1] :

Experiment performed according to the above-described procedure using 10.6 mg (0.010 mmol) of [cinchonidinium][Δ-**1**] salt in 10% DMSO in $CHCl_3$ and 8.0 mg of [**5**]Cl_2 in water. Salt [**5**][Δ-**1**]$_2$ is extracted into the organic layer and obtained as an orange-solid (10.9 mg, 48%). From the aqueous layer, an orange residue is obtained.

Organic layer:



[Ru(4,7-dimethyl-1,10-phenanthroline)$_3$][Δ-1]$_2$ salt or [5][Δ-1]$_2$.

M.p. > 298°C (decomp.). **^{31}P NMR** (162 MHz, 20% [D_6]DMSO in $CDCl_3$): -80.2. **^{1}H NMR** (400 MHz, 20% [D_6]DMSO in $CDCl_3$, d.r. 49:1, only major diastereoisomer is observed): 7.99 (d, ^{3}J=5.5 Hz, 6H, H(2,9)); 7.92 (s, 6H, H(5,6)); 6.80 (d, ^{3}J=5.5 Hz, 6H, H(3,8)); 2.22 (s, 18H, H(Me)). **^{13}C NMR** (100 MHz, 80% [D_6]DMSO in $CDCl_3$): 151.4 (CH, 6C); 146.9 (C, 6C); 146.1 (C, 6C); 141.1 (C, $^2J_{(C\text{-}P)}$=7 Hz, 6C, C(1')); 129.7 (C, 6C); 126.3 (CH, 6C); 124.2 (CH, 6C); 121.8 (C, 6C, C(3')); 113.0 (C, 1 (C, $^3J_{(C\text{-}P)}$=19 Hz, 6C, C(2'); 18.1 (CH_3, 6C, C(Me)). **IR** (CH_2Cl_2): 3052 (m); 2964 (m); 1622 (w); 1453 (w); 1278 (s); 1054 (s); 1033 (s); 1011 (s); 821 (m). **CD** (1% DMSO in CH_2Cl_2, $1.11\cdot10^{-5}$ M, 20°C): λ(Δε) 240.0 (-43); 260.5 (+121); 271.0 (-141); 474.0 (-5). **ES-MS**: (+) 363.1 [$C_{42}H_{36}N_6Ru]^{2+}$; 1494.5 [$C_{42}H_{36}N_6Ru$][TRISPHAT]$^+$; (-) 768.6 [TRISPHAT]$^-$.

[1] The diastereomeric purity of the TRISPHAT salts can be increased by chromatography (SiO_2, CH_2Cl_2) following the previously described procedure: J. Lacour, S. Torche-Haldimann, J. J. Jodry, C. Ginglinger, F. Favarger, *Chem. Commun.* **1998**, 1733-1734.

[2] J. Lacour, C. Ginglinger, F. Favarger, S. Torche-Haldimann, *Chem. Commun.* **1997**, 2285-2286.