Efficient Synthesis of Tris(acetonitrile)-(η^5-cyclopentadienyl)-ruthenium(II) Hexafluorophosphate *via* Ruthenocene

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Abstract: [Ru(η^5-C_5H_5)(CH_3CN)$_3$][PF_6] (**1**), a versatile precursor to catalysts containing the $CpRu^+$ complex fragment, can be obtained in high yield *via* Cp/naphthalene exchange in ruthenocene. This new route *via* the complex [RuCp(naphthalene)][PF_6] (**4**) avoids both highly toxic thallium reagents and the need for a photoreactor.

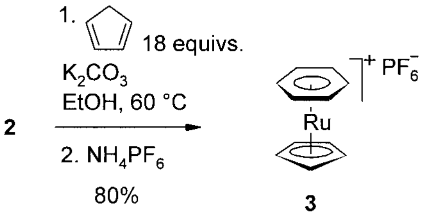
Keywords: arene complexes; cyclopentadienyl ligands; ligand exchange; ruthenium; ruthenocene

The lability of the acetonitrile ligands in [Ru(η^5-C_5H_5)(CH_3CN)$_3$][PF_6] (**1**), tris(acetonitrile)(η-cyclopentadienyl)ruthenium(II) hexafluorophosphate, gives rise to a very rich chemistry.[1] Complex **1** is the precursor of choice for the synthesis of many complexes and catalysts containing the "$RuCp^+$" fragment. Arenes react with **1** under mild conditions, thus providing a high-yield access to cationic [Ru(arene)Cp]$^+$ sandwich complexes in which the arene is activated to nucleophilic addition and substitution reactions.[2] Synthetic applications apart, these compounds are also used in Ru-labeling of biological compounds.[3] Recent studies have revealed **1** to be a pre-catalyst for a number of elegant C–C bond-forming reactions involving alkynes and alkenes.[4] The monophosphine derivative [Ru(η^5-C_5H_5)(CH_3CN)$_2$ PR_3][PF_6] is a catalyst for the isomerization of allylic alcohols to aldehydes and ketones,[5] and this complex has also been used successfully for the study of the mechanism of the coupling reaction of alkenes and alkynes,[6] and for the synthesis of novel Ru(allyl)(carbene)Cp complexes.[1,7] Further applications of cationic RuCp complexes are in the fields of planar chiral Ru-arene complexes[8] and Ru-Lewis acid catalysts.[9]

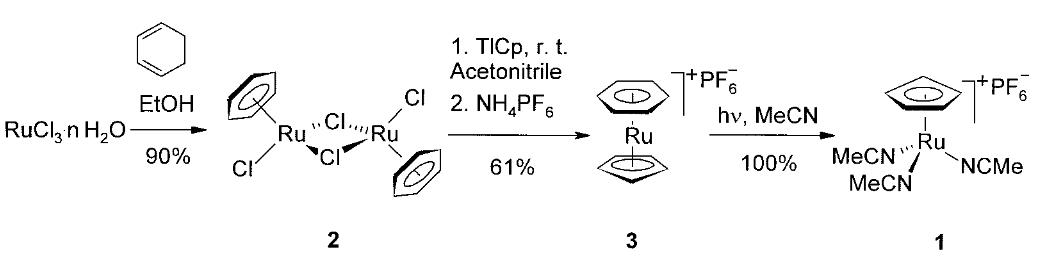
With much useful chemistry firmly established, it is surprising that until very recently, the best route of access to **1** was the three-step procedure first described by Gill and Mann[10] and based on the substitution of chloride in [(Ru(C_6H_6)Cl_2]$_2$[11] by cyclopentadienide using TlCp followed by photolytic Ru-arene bond cleavage (Scheme 1).

In 2002, Trost and Older showed that TlCp could be substituted by cyclopentadiene/K_2CO_3 in EtOH (Scheme 2).[12] This is a substantially improved protocol for the synthesis of the mixed sandwich complex **2** because it avoids the toxic thallium reagent and therefore makes multi-gram synthesis of **3** ecologically feasible. However, the final step, arene substitution by acetonitrile to give **1** still requires irradiation of a solution of **3** in a photoreactor,[13] an inconvenient protocol for larger scale preparations of **1**.

While reviewing the synthesis of π-arene metal complexes,[14] we reflected on the different approaches used for the synthesis of Fe(arene)Cp^+ and



Scheme 2. Improved protocol for the synthesis of **3** according to Trost and Older.[12]



Scheme 1. Synthesis of **1** *via* the Gill and Mann procedure.[10]

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$Ru(arene)Cp^+$ complexes. The former are conveniently prepared from ferrocene using Lewis acid assisted Cp/arene exchange. In contrast, ligand exchange in ruthenocene has up to now not been a practical route to $Ru(arene)Cp^+$ complexes. Rather, these complexes are prepared either directly *via* analogues of **2** or by heating **1** in the presence of the arene. In this article we reexamine the ruthenocene route and present an efficient protocol for Cp/naphthalene exchange in ruthenocene.

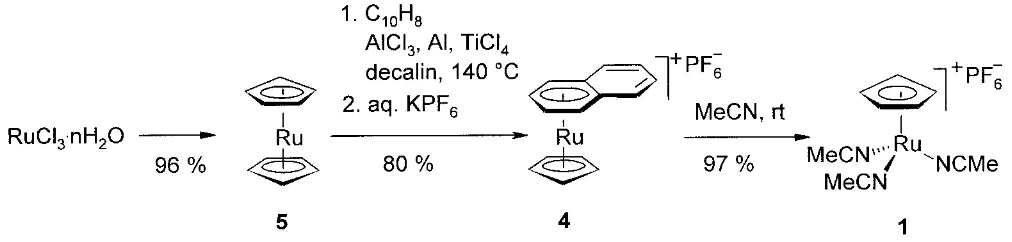
Ruthenocene is more robust than ferrocene[15] and no exchange takes place under the conditions of the ferrocene reactions ($AlCl_3$, Al, methylcyclohexane, 80–100 °C).[16] Raising the temperature to 165 °C does give the arene complexes, albeit in very low yields (5–15% with the arenes benzene, biphenyl, chlorobenzene and naphthalene). Extensive decomposition is predominant under these harsh conditions.[16] The best yield for an arene complex was reported for [RuCp(mesitylene)][PF_6] (30%) and was obtained from a reaction at 165 °C.[16b] This procedure is not synthetically useful. Moreover, the method is not applicable to the synthesis of complexes with less robust Ru-arene bonds such as naphthalene.

We focused attention on the synthesis of [RuCp(naphthalene)][PF_6] (**4**). Naphthalene complexes undergo facile haptotropic slippage[14] and the kinetics of arene displacement in **4** by acetonitrile were studied by McNair and Mann close to 20 years ago.[17] They reported the half-life for the pseudo-first order substitution of naphthalene in **4** by acetonitrile to be *ca.* 4.7 h at 22 °C. The same paper also showed the reverse reaction to be an efficient route to **4**. The naphthalene complex **4** was obtained in 88% yield upon heating **1** in 1,2-dichloroethane in the presence of an excess of naphthalene. This route compares very favorably to that obtained *via* ruthenocene (13%).[16a]

A report in the patent literature on the synthesis of [Fe(arene)Cp][PF_6] claims that the addition of $TiCl_4$ to the reaction (ferrocene/arene/$AlCl_3$/Al/methylcyclohexane) in the proportion ferrocene to $TiCl_4$ = *ca.* 2:1 is beneficial. The titanium reagent traps the cyclopentadienyl ligands to form titanocene dichloride and this can increase the yield of the cationic arene complex by 10–30%.[18] We have successfully used this procedure in the preparation of FeCp(naphthalene) complexes[19] and envisaged its extension to arene exchange in ruthenocene. After some experimentation and variation of temperature and reaction time the following synthesis protocol for complex **4** was established: A suspension of ruthenocene (1 equiv.), naphthalene (10 equivs.), $AlCl_3$ (1 equivs.) and Al powder (0.5 equiv.) and $TiCl_4$ (0.5 equiv.) was heated to 140 °C and stirred for 3 days. After work-up (see Experimental Section) and anion exchange, this procedure afforded [RuCp(naphthalene)][PF_6] (**4**) in 80% yield! The Cp_2TiCl_2 produced in this reaction was not isolated. The use of either $ZrCl_4$ or $HfCl_4$ in place of $TiCl_4$ afforded **4** in lower yields. We briefly checked the $TiCl_4$ procedure with different counter ions in the final step and isolated [RuCp(naphthalene)][X] with X = $CF_3SO_3^-$, SbF_6^-, BF_4^- in 76%, 60%, and 70% yields, respectively.

We next turned our attention to the synthesis of ruthenocene (**5**). Literature reports for the synthesis of **5** from $RuCl_3 \cdot 3\,H_2O$ vary in yield from 75 to 82%. We chose the established procedure of Pertici and Vitulli,[20] reduced the amount of cyclopentadiene to 15 equivs. and replaced benzene as solvent in the work-up by toluene. This, and rigorous exclusion of air, afforded ruthenocene (**5**) in 96% yield (Scheme 3).

Optimization of the final step, the naphthalene displacement in **4** by acetonitrile to give **1**, proved less easy than expected at first. Complex **4** was placed in an excess of freshly distilled, degassed acetonitrile and the progress of the reaction was monitored by removing aliquots that were then analyzed by ^1H NMR. In keeping with the findings by McNair and Mann,[17] the reaction needed no irradiation and proceeded to completion after stirring at room temperature for 35 h. On a preparative scale, it turned out, however, that product **1** was contaminated by small amounts (3–6%) of the naphthalene complex **4**. We concluded that evaporation to dryness and sublimation of liberated naphthalene at room temperature regenerated small quantities of **4**. Most probably the presence of **4** as impurity would not affect reactions but the experimental part details a protocol that avoids this contaminant by extracting liberated naphthalene with hexane from a biphasic hexane-acetonitrile mixture prior to solvent removal. No irradiation is required for the Ru-naphthalene substitution but we noticed that when the pyrex reaction flask is exposed to light from the laboratory fluorescent tubes or to sunlight, the reaction is accelerated.



Scheme 3. The new ruthenocene route to **1**.

In summary, we here detail an operationally safe and simple method for the synthesis of the title complex **1** that avoids both special apparatus and highly toxic reagents. In contrast to previous methods, the Cp ligand is introduced prior to the arene, thus foregoing the need for a Birch reduction of the arene. The key step is the Cp/arene exchange in ruthenocene and the spectacular improvement of the yield of this transformation over earlier reports is due to the addition of $TiCl_4$ to the reaction mixture. The choice of naphthalene as arene is dictated by the ease of substitution of this arene by acetonitrile. This final step does not require photolysis apparatus. This and the fact that neither chromatography nor special purification of intermediates is necessary makes this synthesis protocol truly suitable for the large-scale production of the valuable complex $[Ru(\eta^5\text{-}C_5H_5)(CH_3CN)_3][PF_6]$ (**1**).

Experimental Section

General Remarks

Reactions and manipulations were carried out under N_2 by using an inert gas/vacuum double manifold and standard Schlenk techniques. $RuCl_3 \cdot n\,H_2O$ was purchased from Pressure Company. Naphthalene was purchased from Merck; Zn, Al, $TiCl_4$, KPF_6, $AgCF_3SO_3$ from Fluka; and $NaBF_4$, $AlCl_3$, $NaSbF_6$ were obtained from Acros. All of the above were used as received. CH_3CN and toluene were dried using passage through activated Al_2O_3[21] and degassed by passing N_2 through the solvent or by successive freeze, pump, thaw cycles (2 to 3). Melting points were determined on a Büchi 510 apparatus and are not corrected. IR spectra were recorded on a Perkin-Elmer 1600 FT-IR spectrometer by means of a Golden Gate© accessory. NMR spectra (^1H at 300 or 400 MHz, ^{13}C at 75.5 or 100.5 MHz, ^{31}P at 162 MHz) were recorded at room temperature on a Bruker 300 MHz or a Bruker 400 MHz spectrometer as indicated. Chemical shift (δ) are reported relative to TMS for ^1H and ^{13}C spectra and to H_3PO_4 for ^{31}P spectrum, and are expressed in ppm. MS data were obtained on a Finnigan SSQ 7000 spectrometer; *m/z* (intensity in %). Elemental analyses were carried out by H. Eder, Service de Microchimie, Institut de Chimie Pharmaceutique, Université de Genève.

Ruthenocene $[Ru(\eta^5\text{-}C_5H_5)_2]$ (5)[20]

A Schlenk tube (200 mL) equipped with a magnetic stirring bar was charged with ruthenium trichloride (5.26 g, 0.02 mol) and absolute ethanol (80 mL). Cyclopentadiene (25 mL, 0.3 mol) was added to the dark red-black solution followed by zinc dust (13 g, 0.2 mol, added in five portions). The reaction mixture turned rapidly dark blue, and then, more slowly, dark grey. After stirring for 2 hours at room temperature (r.t.), the mixture was filtered on a G3 glass sinter in air. The metallic grey solid was washed with toluene (4 × 15 mL) and the filtrate was evaporated to dryness. The dark solid residue was then taken up in toluene (500 mL) and passed through a plug of silica gel (100 × 15 mm). The resulting clear solution was evaporated to dryness to afford **5** as white crystalline solid; yield: 4.45 g (96%); mp 197–200 °C (ref.[20] 199–200 °C); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 4.59$ (s); ^{13}C NMR (100.5 MHz, $CDCl_3$): $\delta = 70.1$; anal. calcd. for $C_{10}H_{10}Ru$ (231.259): C 51.93, H 4.36; found: C 51.92, H 4.38.

$[Ru)(\eta^5\text{-}C_5H_5)(\eta^6\text{-}C_{10}H_8)][PF_6]$ (4)[16]

Ruthenocene (**5**; 4.42 g, 19 mmol), naphthalene (24 g, 190 mmol), aluminium trichloride (2.55 g, 19 mmol) and Al powder (0.258 g, 9.5 mmol) were placed in a Schlenk tube (300 mL) equipped with a magnetic stirring bar. Dry, N_2-saturated decalin (150 mL) was added under a nitrogen atmosphere followed by titanium tetrachloride (1.04 mL, 9.5 mmol, added dropwise *via* syringe at 40 °C). The temperature of the dark reaction mixture was then raised to 140 °C and the mixture stirred at this temperature for 3 days. After cooling to r.t., a mixture of iced water (300 g), 30% hydrochloric acid (25 mL) and 32% hydrogen peroxide (25 mL) was added. The resulting mixture was thoroughly mixed for 5 min, the aqueous phase was separated, and the organic phase extracted with small portions of water. Addition of KPF_6 (5.2 g, 0.0285 mol) to the combined aqueous phase precipitated a light yellow solid. Extraction with dry, N_2-saturated CH_2Cl_2 (5 × 100 mL), combination of the organic layers, drying over Na_2SO_4, filtration and evaporation to dryness afforded **4** as pale orange solid; yield: 6.70 g (80%); mp 155–160 °C (dec.); ^1H NMR (400 MHz, acetone-d_6): $\delta = 5.15$ (s, 5H), 6.47–6.48 (m, 2H), 7.24–7.25 (m, 2H), 7.70–7.73 (m, 2H), 7.89–7.92 (m, 2H); ^{13}C NMR (100.5 MHz, acetone-d_6): $\delta = 79.7$, 83.9, 85.9, 97.2, 129.3, 131.5; ^{31}P NMR (162 MHz, acetone-d_6): $\delta = -144.1$ (sept, PF_6); FT-IR: $\nu = 3122$, 1630, 1530, 1412, 818, 554 cm^{-1}; MS (ESI): *m/z* = 295 ($[M]^+ + H$, 100); anal. calcd. for $C_{15}H_{13}F_6PRu$ (439.3021): C 41.01, H 2.98; found: C 41.66, H 3.35.

$[Ru(\eta^5\text{-}C_5H_5)(CH_3CN)_3][PF_6]$ (1)[10,12]

The naphthalene complex **4** (13.7 mmol, 6 g) was placed in a Schlenk tube (200 mL) equipped with a magnetic stirring bar. Dry, N_2-saturated acetonitrile (60 mL) was added under N_2. The pale yellow-orange solution was stirred at r.t. After 24 h, hexane (50 mL) was added, the solution was vigorously stirred for 5 minutes and then the upper phase of the biphasic system was decanted. This process was repeated twice with the last mL of the hexane layer being removed by a syringe. Stirring of the acetonitrile solution was continued for another 24 h followed by a second extraction by hexane (3 × 50 mL). After a total of 53 h stirring, the dark orange acetonitrile solution was taken to dryness in a vacuum. The resulting orange-yellow solid was washed with hexane (3 × 50 mL) to give **1** as an orange powder; yield: 5.75 g (97%);^1H NMR (400 MHz, acetone-d_6): $\delta = 4.25$ (s, 5H), 2.44 (s, 9H); ^{13}C NMR (100.5 MHz, acetone-d_6): $\delta = 2.4$, 68.6, 125.9; FT-IR: $\nu = 2282$, 1412, 1032, 830, 556 cm^{-1}.

Acknowledgements

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