A Convenient Synthetic Route to $[CpRu(CH_3CN)_3]PF_6$

Barry M. Trost* and Christina M. Older

Department of Chemistry, Stanford University, Stanford, California 94305-5080

Received February 20, 2002

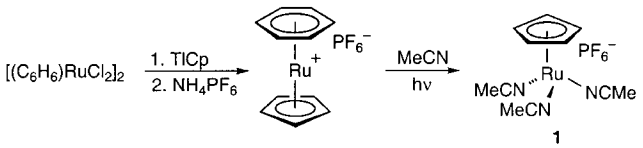
Summary: A new practical protocol that avoids the stoichiometric use of either thallium or silver salts for the synthesis of the title compound is described.

Introduction

The chemistry of cyclopentadienylruthenium complexes has historically been based on the readily available $CpRu(PPh_3)_2Cl$ and $CpRu(CO)_2Cl$ precursors. However, the selective displacement of CO or PPh_3 has proved difficult, limiting the synthetic utility of these systems. The cationic complex $[CpRu(CH_3CN)_3]PF_6$ (**1**) has currently gained in popularity as an alternative entry to cyclopentadienylruthenium complexes due to the substitutional lability of the CH_3CN ligands.[1] The high affinity of the $CpRu^+$ fragment for arene rings has also led to the application of **1** in Ru-promoted nucleophilic aromatic substitution reactions[2] and in Ru-labeling of biological compounds.[3] The catalytic properties of $[CpRu(CH_3CN)_3]PF_6$ for a variety of C−C bond forming reactions have only recently been examined and include (a) the dimerization of propargyl alcohols,[4] (b) regioselective alkene−alkyne coupling,[5] (c) intramolecular [5+2] cycloaddition of alkyne−vinylcyclopropanes,[6] (d) cycloisomerization of 1,6- and 1,7-enynes,[7] and (e) cyclopropanation of norbornene with propargyl alcohol.[8]

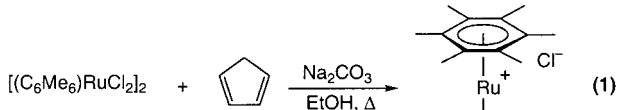
The synthesis of **1**, first reported by Gill and Mann in 1982,[9] is a three-step process starting from readily available $[(C_6H_6)RuCl_2]_2$ and is shown in Scheme 1. Although the preparation of cationic **1** is straightforward, the use of stoichiometric thallium (or silver) to introduce the cyclopentadienyl moiety to form $[(C_6H_6)RuCp]PF_6$ (**2**)[10a,b] (or its tetrafluoroborate salt[10c]) is problematic for large-scale reactions. The high toxicity of thallium and the subsequent disposal of thallium waste make this procedure unattractive for many organic chemists. The transmetalation reaction is also very sensitive to the quality of the thallium cyclopentadienide. In this note we wish to report an extremely facile and economical synthesis of $[(C_6H_6)RuCp]PF_6$ via the ethanolic reduction of $[(C_6H_6)RuCl_2]_2$ in the presence of excess cyclopentadiene.

Scheme 1



Results and Discussion

Early work by Bennett had demonstrated that $(C_6Me_6)Ru(0)$ diene complexes could be synthesized by treatment of ethanolic $[(C_6Me_6)RuCl_2]_2$ with sodium carbonate and excess diene.[11] More recently, Stryker has used similar conditions to prepare $[(C_6Me_6)RuCp]Cl$ in good yield (eq 1).[12] It appears that, in the case of cyclopentadiene, the thermodynamic product of the ethanolic reduction is the Ru(II) cyclopentadienyl complex rather than the Ru(0) diene, suggesting a convenient entry to cyclopentadienylruthenium complexes. Although this reaction proceeds cleanly from the hexamethylbenzene dimer, decomplexation of this electron-rich arene is difficult.[13]



Treatment of $[(C_6H_6)RuCl_2]_2$ under the conditions reported by Bennett[11a] affords only a moderate yield (28%) of the desired $[(C_6H_6)RuCp]PF_6$ (**2**) after ion exchange. (The initial product, $[(C_6H_6)RuCp]Cl$, is converted to the hexafluorophosphate salt to aid in isolation of the complex.) The low yield is attributed to the formation of significant amounts of ruthenocene as a byproduct. Initial optimization of the reaction conditions increased the yield of **2** to 45%, but the amount of Cp_2-

(1) Recent review of $[CpRu(CH_3CN)_3]^+$ chemistry: Slugovc, C.; Rüba, E.; Schmid, R.; Kirchner, K.; Mereiter, K. *Monatsh. Chem.* **2000**, *131*, 1241.

(2) (a) Pigge, F. C.; Fang, S. *Tetrahedron Lett.* **2001**, *42*, 17. (b) Pearson, A. J.; Heo, J.-N. *Tetrahedron Lett.* **2000**, *41*, 5991. (c) Pearson, A. J.; Belmont, P. O. *Tetrahedron Lett.* **2000**, *41*, 1671. (d) Pearson, A. J.; Zhang, P.; Lee, K. *J. Org. Chem.* **1996**, *61*, 6581.

(3) (a) Jaouen, G.; Vessieres, A.; Buttler I. S. *Acc. Chem. Res.* **1993**, *26*, 361. (b) Soine W. H.; Guyer, C. E.; Knapp, F. F. *J. Med. Chem.* **1984**, *27*, 803.

(4) Trost, B. M.; Rudd, M. T. *J. Am. Chem. Soc.* **2001**, *123*, 8862.

(5) (a) Trost, B. M.; Surivet, J.-P.; Toste, F. D. *J. Am. Chem. Soc.* **2001**, *123*, 2897. (b) Trost, B. M.; Pinkerton, A. B.; Toste, F. D.; Sperrle, M. *J. Am. Chem. Soc.* **2001**, *123*, 12504. (c) Trost, B. M.; Brown, R. E.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 5877. (d) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 714.

(6) (a) Trost, B. M.; Toste, F. D.; Shen, H. C. *J. Am. Chem. Soc.* **2000**, *122*, 2379. (b) Trost, B. M.; Shen, H. C. *Org. Lett.* **2000**, *2*, 2523.

(7) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **2000**, *122*, 714.

(8) Matsushima, Y.; Kikuchi, H.; Uno, M.; Takahashi, S. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 2475.

(9) Gill, T. P.; Mann, K. R. *Organometallics* **1982**, *1*, 485.

(10) (a) Zelonka, R. A.; Baird, M. C. *J. Organomet. Chem.* **1972**, *44*, 383. (b) Zelonka, R. A.; Baird, M. C. *J. Can. Chem.* **1972**, *50*, 3063. (c) Oshima, N.; Suzuki, H.; Morooka, Y. *Inorg. Chem.* **1986**, *25*, 3407.

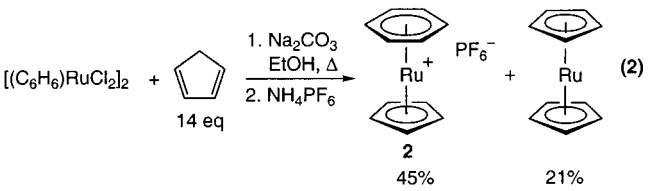
(11) (a) Bennett, M. A.; Huang, T.-N.; Matheson, T. W.; Smith, A. K. *Inorg. Synth.* **1982**, *21*, 74. (b) Bennett, M. A.; Matheson, T. W. *J. Organomet. Chem.* **1978**, *153*, C25. (c) Bennett, M. A.; Huang, T.-N.; Turney, T. W. *J. Chem. Soc., Chem. Commun.* **1979**, 312.

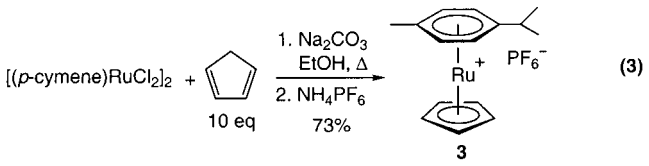
(12) Older, C. M.; Stryker, J. M. *J. Am. Chem. Soc.* **2000**, *122*, 2784.

(13) Nolan, S. P.; Marthin, K. L.; Stevens, E. D.; Fagan, P. J. *Organometallics* **1992**, *11*, 3947.

10.1021/om020143p CCC: $22.00
Publication on Web 05/15/2002

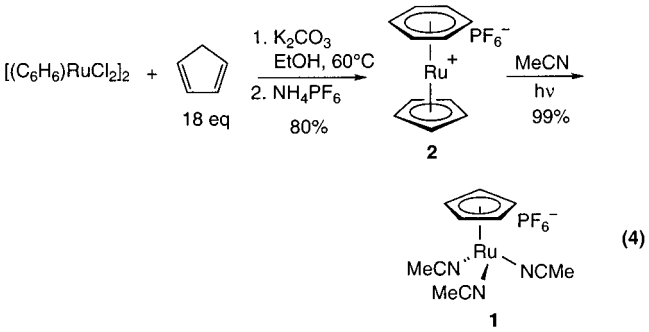
Ru produced remained at ~20%, even after short reaction times (eq 2).





However, switching to the alternative precursor, [(*p*-cymene)$RuCl_2]_2$, resulted in much better yields of the cyclopentadienyl complex **3**, with no traces of the ruthenocene byproduct being detected (eq 3).[14] Unfortunately this complex, unlike its benzene analogue, was usually isolated as an oil or an oily solid from this reaction. Only after purification by chromatography could it be obtained as a pure crystalline material, a disadvantage for large-scale reactions. An even bigger obstacle was encountered when [(*p*-cymene)RuCp]PF_6 was subjected to photolysis in acetonitrile. Although NMR spectroscopy of the crude material indicated near-quantitative conversion to the expected [CpRu$(CH_3CN)_3$]-PF_6, the oily product refused to crystallize even after repeated filtration through alumina. Moreover, this material was quite air-sensitive and rapidly turned black on the bench. It is probable that residual *p*-cymene inhibits the crystallization of the tris(acetonitrile) **1**, which is susceptible to air-oxidation when not in solid form.

Because of these difficulties with the *p*-cymene system, it was decided to reexamine the reaction conditions for the parent $[(C_6H_6)RuCl_2]_2$. It was soon found that the choice of alcohol and base was crucial for this reaction. Ethanol proved to be the best alcohol; use of refluxing 2-propanol yielded only a small amount of [(C_6H_6)RuCp]PF_6, while methanol returned no tractable product. Of the bases screened, zinc dust yielded results similar to those for sodium carbonate, while cesium carbonate resulted in very low conversion. Potassium carbonate, however, was found to give good yields of **2** with negligible amounts of the ruthenocene byproduct (2−3%). Lowering the reaction temperature from that of refluxing ethanol to 60 °C with a concomitant increase in reaction time afforded a slightly cleaner product in ~80% yield. The optimized conditions thus consist of treating $[(C_6H_6)RuCl_2]_2$ with excess cyclopentadiene and potassium carbonate in anhydrous ethanol at 60 °C for 7 h (eq 4). The reaction mixture is then filtered to remove excess potassium carbonate, followed by addition of an aqueous solution of NH_4PF_6. Removal of the ethanol solvent results in the precipitation of crude [(C_6H_6)RuCp]PF_6, which can be further purified by recrystallization from acetone/diethyl ether if desired. This reaction has been conducted on a 7.5 g (15 mmol) scale of $[(C_6H_6)RuCl_2]_2$ with similar results, indicating that multigram scale reactions are feasible. Irradiation of an acetonitrile solution of **2** prepared by this method results in its quantitative conversion to [CpRu$(CH_3CN)_3$]-PF_6, which is isolated as a spectroscopically pure orange solid after concentration of the crude reaction mixture.



Conclusion

Introduction of the cyclopentadienyl ligand via ethanolic reduction of [(arene)$RuCl_2]_2$ in the presence of cyclopentadiene is a simple and convenient entry to cyclopentadienylruthenium complexes. Since the described route avoids the need for purification by chromatography at any stage, it is particularly amenable to large-scale production. This methodology thus represents a significant improvement over the literature synthesis by avoiding toxic thallium or expensive silver reagents while maintaining operational simplicity.

Experimental Section

General Comments. $[(C_6H_6)RuCl_2]_2$ was prepared from $RuCl_3 \cdot H_2O$ and 1,3-cyclohexadiene according to the described procedure.[15] Fresh commercial anhydrous ethanol was used without further purification and was deoxygenated by bubbling a stream of dry nitrogen through it for 10 min prior to cannula transfer to the reaction flask. All other solvents were purified by standard methods before use.

Synthesis of $[(C_6H_6)Ru(C_5H_5)]PF_6$ (2). A 100 mL oven-dried round-bottom flask equipped with a stir-bar was charged with finely ground potassium carbonate (1.95 g, 14.2 mmol, 6.0 equiv) and the flask flame-dried under vacuum. After cooling to room temperature, the flask was further charged with $[(C_6H_6)RuCl_2]_2$ (1.18 g, 2.36 mmol) and a reflux condensor added. Ethanol (50 mL) was then added, followed by freshly cracked cyclopentadiene (3.5 mL, 42.4 mmol, 18 equiv). The resulting heterogeneous brown mixture was then warmed to 60 °C with rapid stirring. After approximately 7 h, the reaction mixture was cooled to room temperature and filtered through a plug of Celite, and the Celite rinsed with a further 40 mL of ethanol. The dark yellow filtrate was concentrated to ~20 mL, then an aqueous solution of NH_4PF_6 (1.6 g, 9.8 mmol, 4.16 equiv, in 16 mL of H_2O) was added, resulting in the immediate formation of a tan precipitate. The remaining ethanol was removed under reduced pressure and the resulting suspension cooled for several hours. The mixture was then filtered and the tan solid dried under vacuum to yield 1.45 g (79%). The crude product was subsequently dissolved in a minimum of acetone and diethyl ether added dropwise until precipitate formation was no longer observed. This mixture was cooled for several hours before being filtered to afford 1.36 g (74%) of a white powder. The product is spectroscopically identical to the known $[(\eta^6\text{-}C_6H_6)Ru(C_5H_5)]PF_6$[9] and is pure by ^1H NMR spectroscopy to the limits of detection.

(14) Stephenson, T. A.; Robertson, I. W.; Tocher, D. A. *J. Organomet. Chem.* **1982**, *228*, 171.

(15) Bennett, M. A.; Smith, A. K. *J. Chem. Soc., Dalton Trans.* **1974**, 233.

Synthesis of $[CpRu(CH_3CN)_3]PF_6$ (1). This reaction is a modification of the existing literature procedure.[9] A solution of $[(C_6H_6)Ru(C_5H_5)]PF_6$ (1.70 g, 4.37 mmol) in acetonitrile (200 mL) was prepared in a 250 mL quartz photolysis reactor unit (Ace) and the solution deoxygenated by bubbling a stream of dry nitrogen through it for 30 min. The stirred solution was then irradiated with the output of a 450 W Ace medium-pressure Hg lamp for 12 h. Evaporation of the solvent yielded 1.89 g (>99%) of **1** as a free-flowing, bright orange powder, which is pure by ^1H NMR spectroscopy to the limits of detection.

Acknowledgment. We thank the U.S. National Science Foundation for their generous support of our programs and the Canadian National Science and Engineering Research Council for a postdoctoral fellowship to C.M.O. for partial support.

OM020143P