Synthesis of (η^5-C_5Me_5)Ru(η^6-tryptamine)(CF_3SO_3) Complexes. Chemospecific η^6 Coordination of the (η^5-C_5Me_5)Ru^+ Moiety

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Received September 21, 1993®

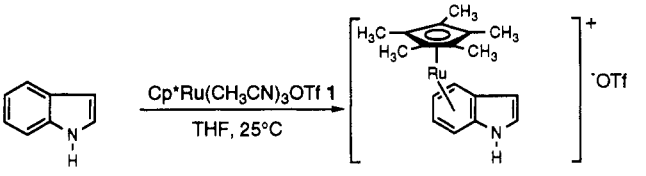
A series of Cp*Ru(η^6-N_b-acyltryptamine)OTf and Cp*Ru(η^6-N_b-CBZ-tryptamine)OTf complexes have been prepared from the reaction of Cp*Ru(CH_3CN)$_3$OTf (1) with the corresponding N_b-acyl-tryptamine and N_b-CBZ-tryptamine derivatives in THF at ambient reaction conditions under an argon atmosphere. The complexes are air stable and were obtained in high yields (>90%). Cp*Ru(η^6-N_b-BOC-tryptamine]OTf (10) and Cp*Ru(η^6-N_b-CBZ-tryptamine)OTf (16) were readily converted into Cp*Ru(η^6-tryptamine)OTf (3) in good yields (61% and 87%, respectively). The kinetic η^6 coordination of the electrophilic Cp*Ru^+ moiety was found to be chemospecific for the electron-rich indole nucleus. No competing η^6 coordination was observed at the arene unit of a variety of substituted N_b-CBZ-tryptamine derivatives.

Introduction

The coordination of transition metals to indole in an η^6 fashion is well documented throughout the literature. Transition-metal systems which employ chromium[1-3] and ruthenium[4] have received the greatest amount of attention and have been proven to be synthetically useful. However, cobalt, iridium, and rhodium complexes of indole are also known.[5,6] Despite the numerous studies in the area of η^6 transition-metal indole complexes it is surprising that there have been no reports with regard to the synthesis and/or chemistry of η^6 transition-metal indole complexes of higher order indole derivatives such as tryptamine and tryptophan. As part of a continuing program in our laboratories focused toward the synthesis of tryptamine-related alkaloids, it was our objective to develop a method for the synthesis of η^6 transition-metal tryptamine complexes. In light of the known chemistry of η^6 transition-metal indole complexes the availability of η^6 transition-metal tryptamine complexes would undoubtedly prove useful for the preparation of complex tryptamine derivatives.

In choosing a transition-metal system for the synthesis of η^6 transition metal tryptamine complexes, we first felt that the system must meet three specific criteria. First, since the η^6 transition-metal tryptamine complexes are to be ultimately employed as synthetic intermediates, the formation of the complex must proceed in high yield under mild conditions in the presence of a variety of functional groups. Second, the coordination step of the metal to the tryptamine ligand must be amenable to at least moderate-scale preparations to furnish useful quantities of stable, easily handled organometallic compounds. Finally, the removal of the metal must be facile and preferably provide the metal in a recoverable useful chemical state.

Previous work by Moriarty and co-workers demonstrated that 4- and 5-substituted CpRu(η^6-indole)PF_6 derivatives are versatile synthetic intermediates for the preparation of a variety of indole derivatives.[4,7] Moreover, it was shown that the CpRu moiety could be photochemically cleaved in acetonitrile to regenerate the CpRu(CH_3CN)$_3$$PF_6$ complex and furnish the chemically altered indole.[7,8] We have also recently shown in these laboratories that Cp*Ru(CH_3CN)$_3$OTf (1; (Cp* = C_5Me_5; OTf = $CF_3SO_3^-$) reacts with a variety of arenes to furnish remarkably stable Cp*Ru(η^6-arene)OTf complexes, including Cp*Ru(η^6-indole)OTf (2), in exceptionally high



2 (98% yield)

yields (>90% yield).[9,10] Therefore, on the basis of these aspects of organoruthenium chemistry, we felt that the Cp*Ru system would be ideal for the synthesis of η^6 transition-metal tryptamine complexes. Herein we describe results from our studies directed toward the synthesis of Cp*Ru(η^6-tryptamine) complexes.

Results and Discussion

Direct extension of the known chemistry of Cp*Ru(CH_3CN)$_3$OTf (1) with indole to a tryptamine (trypt) system for the synthesis of Cp*Ru(η^6-trypt)OTf (3) was not obvious at first.[9,10] The reactivity of the nucleophilic N_b nitrogen atom versus the six electron arene π system

® Abstract published in *Advance ACS Abstracts,* January 1, 1994.

(1) Fischer, E. O.; Goodwin, H. A.; Kriefer, C. G.; Simmons, H. D.; Sonogashira, J.K.; Wild, J. B. *J. Organomet. Chem.* **1968**, *14*, 359.
(2) (a) Semmelhack, M. F.; Clack, G. R.; Harrison, J. L.; Thebtaranonth, Y.; Wulff, W. *Tetrahedron* **1981**, *23*, 3957. (b) Semmelhack, M. F.; Wulff, W.; Garcia, J. L. *J. Organomet. Chem.* **1982**, *240*, C5.
(3) (a) Beswick, P. J.; Greenwood, C. S.; Mowlem, T. J.; Nechvatal, G.; Widdowson, D.A. *Tetrahedron* **1988**, *44*, 7325. (b) Nechvatal, G.; Widdowson, D. A. *J. Chem. Soc., Chem. Commun.* **1982**, 447.
(4) For a recent review see: Gill, U. S.; Moriarty, R. M.; Ku, Y. Y.; Butler, J. R. *J. Organomet. Chem.* **1991**, *417*, 313.
(5) Fairhurst, G.; White, C. *J. Chem. Soc., Dalton Trans.* **1979**, 1531.
(6) White, C.; Thompson, S. J.; Maitlis, P. M. G. *J. Chem. Soc. Dalton Trans.* **1987**, 1654.
(7) (a) Moriarty, R. M.; Ku, Y. Y.; Gill, U. S. *J. Chem. Soc., Chem. Commun.* **1987**, 1493. (b) *Organometallics* **1988**, *7*, 660.
(8) Gill, T. P.; Mann, K. R. *Organometallics* **1982**, *1*, 485.
(9) Nolan, S. P.; Martin, K. L.; Stevens, E. D.; Fagan, P. J. *Organometallics* **1992**, *11*, 3947.
(10) Nolan, S. P.; Martin, K. L.; Buzatu, D.; Trudell, M. L.; Stevens, E. D.; Fagan, P.J. *Struct. Chem.* **1993**, *64*, 373.

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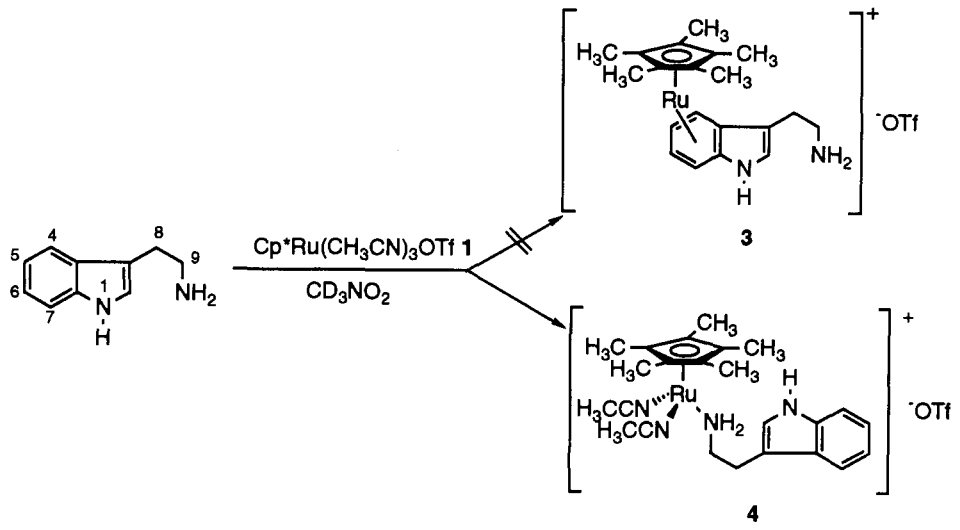
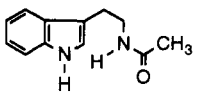
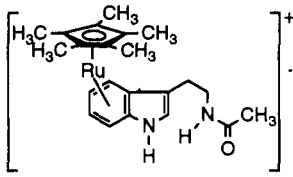
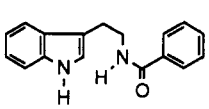
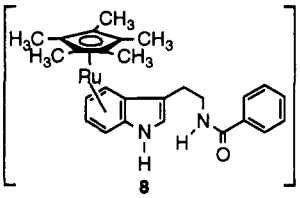
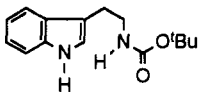
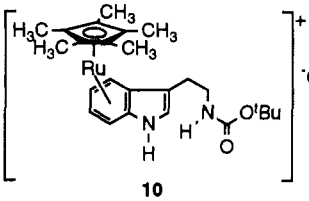
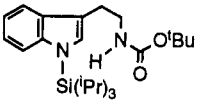
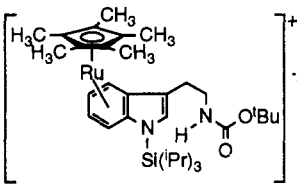
Scheme 1



had to be addressed. It was not clear from previous studies involving arene coordination of 1 whether the nucleophilic lone pair of electrons on the N_b nitrogen atom of tryptamine would inhibit η^6 coordination of the Cp*Ru$^+$ moiety to the indole ring. As an introduction to this system we explored the possibility of preparing **3** by direct coordination of the Cp*Ru$^+$ moiety to the indole nucleus by the reaction of **1** with tryptamine. As illustrated in Scheme 1, NMR studies revealed that treatment of tryptamine with 1 equiv of **1** in CD_3NO_2 at room temperature under an argon atmosphere did not yield Cp*Ru(η^6-tryptamine)OTf (**3**), but rather afforded the metastable Cp*Ru(tryptamine)$(CH_3CN)_2$OTf (**4**). It was obvious from ^{1}H NMR analysis that coordination of the ruthenium metal center had taken place at the lone pair of electrons on the N_b nitrogen atom over η^6 coordination to the indole π system; the methylene signals were deshielded relative to those of tryptamine (δ 5.6 (H8) and 6.4 ppm (H9)), while signals of the carbocyclic protons (characteristically shielded in η^6-coordinated indoles) were not affected.[3,7,9] Attempts to convert the σ complex into the entropically favored Cp*Ru(η^6-trypt)OTf proved to be futile; only Cp*Ru(trypt)$(CH_3CN)_2$OTf (**4**) was observed, where extensive decomposition of the complex **4** was observed after extended reaction times and at higher temperatures. The choice of reaction solvent (CD_3NO_2, acetone-d_6, THF-d_8, $CDCl_3$) had no effect on the outcome of the initial coordination step or subsequent conversion attempts.

Synthesis of Cp*Ru(η^6-N_b-acyltrypt)OTf Derivatives. In order to effect the η^6 coordination of the electrophilic Cp*Ru$^+$ moiety to the indole ring, it was necessary to reduce the nucleophilicity of the tryptamine N_b nitrogen atom. This was achieved by conversion of tryptamine into an appropriate amide or carbamate derivative.[11] Treatment of the N_b-acyltryptamine derivatives with Cp*Ru$(CH_3CN)_3$OTf (**1**) in a stirred solution of dry THF at room temperature (2 h) under an argon atmosphere furnished the desired Cp*Ru(η^6-N_b-acyltrypt)-OTf derivatives in high yield (Table 1).[12] The synthesis of tryptamine complex **12** was of particular interest, since Widdowson and co-workers had demonstrated in the chromium tricarbonyl system $Cr(CO)_3$(η^6-indole) that the triisopropylsilyl group was useful for blocking the 2- and 7-positions of indole toward alkylation.[3] This allowed regiospecific alkylation at the 4-position of the indole nucleus. It is notable that the bulky triisopropylsilyl group does not inhibit the η^6 coordination of the large Cp*Ru$^+$

Table 1. Cp*Ru(η^6-N_b-acyltrypt)OTf Derivatives[a]

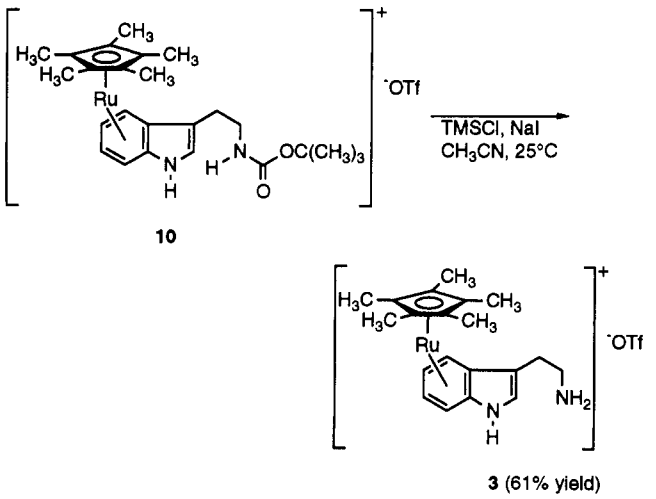
N_b-acyltrpt	Cp*Ru(η^6-N_b-acyltrypt)OTf	yield, %[b]
		92
5	6	
		93
7	8	
		95
9	10	
		96
11	12	

[a] All compounds were prepared using the general procedure described in the Experimental Section. [b] Isolated yields of purified compounds.

(11) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991; pp 315–361 and references cited therein.

(12) The Cp*Ru(η^6-N_b-acyl-trypt)OTf and Cp*Ru(η^6-N_b-CBZ-trypt)-OTf complexes were found to be air-stable but hygroscopic materials. Although the complexes can be easily handled in a dry atmospheric environment, we generally handled and stored the complexes under an argon atmosphere to avoid contact with atmospheric moisture and thus prevent the formation of amorphous gummy material.

Scheme 2



moiety; however, in the ^{1}H NMR spectrum of **12**, the methyl signals of the triisopropylsilyl group were resolved into two distinct doublets at δ 1.05 and 1.14 ppm, respectively, while the ^{13}C signals for the methyl carbon atoms were at δ 12.7 and 10.3 ppm. These NMR data indicate that the methyl groups are diastereotopic, which must result from the asymmetry introduced by the bulky η^6-coordinated Cp*Ru moiety.

Synthesis of Cp*Ru(η^6-trypt)OTf (3). With the complexes in hand, our attention turned toward the deprotection of the N_b protecting group to provide Cp*Ru-(η^6-trypt)OTf (**3**). It was important for the future of these complexes as synthetic intermediates in our work that the protecting groups be easily removed to unmask the nucleophilic N_b nitrogen atom for subsequent use in Pictet–Spengler and related reactions.[13] As originally anticipated, deprotection of the amide derivatives **6** and **8** met with little success. Acid hydrolysis of the amides (HCl, Δ) led to decomposition of the complex. In addition, attempted cleavage of the BOC group of **10** with trifluoroacetic acid at 0 °C led to decomposition of the complex. These results indicate that the Cp*Ru(η^6-trypt)OTf derivatives are sensitive to strong acidic conditions and alternative deprotection conditions should be utilized. As shown in Scheme 2, we found that the BOC group of **10** could be cleaved under aprotic anhydrous conditions with trimethylsilyl iodide generated *in situ* from TMS-Cl (NaI/CH_3CN/25 °C).[14] This furnished the Cp*Ru(η^6-trypt)-OTf (**3**) in 61% yield as a viscous oil. Purification of complex **3** proved to be very difficult due to low solubility in most organic solvents and its extremely hygroscopic nature.

Chemospecific η^6 Coordination of the Cp*Ru$^+$ Moiety to the Indole Nucleus. At this point we were compelled to attempt to improve upon the yield Cp*Ru-(η^6-trypt)OTf (**3**) in order to exploit this chemistry in future syntheses. Therefore, our attention turned toward the development of an alternative protecting group strategy for the N_b amine, which would permit a more facile cleavage of the protecting group under neutral reaction conditions in high yield (<90%). With this criterion in mind, the use of benzyl carbamate (CBZ) derivatives as protecting groups was envisaged. These protecting groups could be removed under anhydrous hydrogenolysis conditions.[11]

At the onset of this study it was not clear to what degree η^6 coordination of the electrophilic Cp*Ru$^+$ moiety to indole would be favored over the phenyl ring of the electronically neutral *O*-benzyl unit (σ_p = 0.06)[15] of the CBZ group. It was clear from our initial studies for the preparation of complex **8** that η^6 coordination of the Cp*Ru$^+$ moiety to the electron-rich indole was favored over coordination to the electron-deficient acyl arene (σ_p = 0.36)[15] of **7**. Similar selectivity has also been demonstrated by Jaouen and co-workers, where η^6 coordination of the Cp*Ru$^+$ moiety to an electronically neutral arene was favored over an electron-deficient arene.[16] However, at the time it was uncertain whether the η^6 coordination of the Cp*Ru$^+$ moiety would differentiate between an electronically neutral arene and an electron-rich arene, since independently both arenes could form stable complexes with the Cp*Ru$^+$ moiety.[9,10] Therefore, in order to facilitate the η^6 coordination of indole, we chose to first look at the *p*-NO_2-CBZ unit (σ_p = 0.81)[15] as a possible protecting group. Treatment of the *p*-NO_2-CBZ-tryptamine species **13** with 1 equiv of **1** under standard reaction conditions afforded the desired Cp*Ru[η^6-N_b-(*p*-NO_2-CBZ)-trypt]OTf (**14**) as a green oil in 91% yield (Table 2). As originally predicted, the η^6 coordination of the Cp*Ru$^+$ moiety to the electron-rich indole ring was chemospecific, with no observable coordination to the arene of the *p*-NO_2-CBZ group.

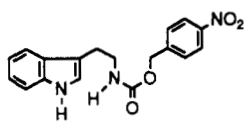
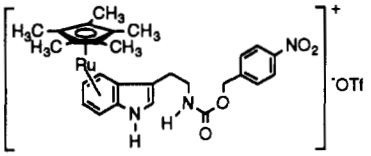
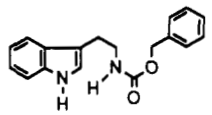
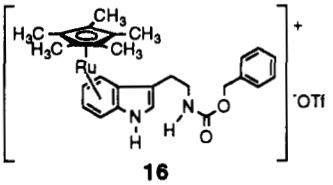
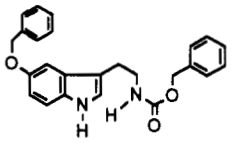
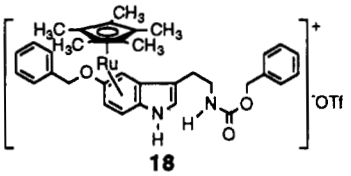
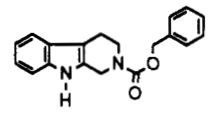
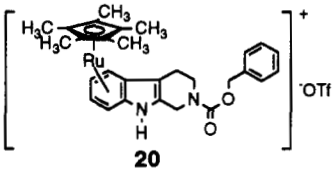
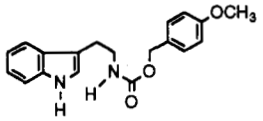
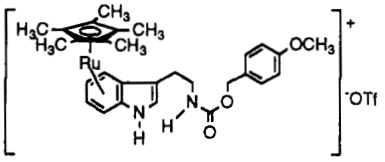
With the complex **14** in hand, the removal of the carbamate unit to provide the free primary amine was explored. Hydrogenolysis of the *p*-NO_2-CBZ unit of **14** was achieved in a solution of dry MeOH using 10% palladium on carbon under an atmosphere of hydrogen (H_2, 1 atm; Scheme 3). This afforded the desired Cp*Ru-(η^6-trypt)OTf (**3**) in quantitative yield, as determined by NMR. Unfortunately, Cp*Ru(η^6-trypt)OTf (**3**) could not be easily isolated in pure form. The nonvolatile side product of the hydrogenation reaction (4-methylaniline) made purification of the hygroscopic complex extremely difficult and furnished **3** in a moderate 53% yield. Since this was obviously no improvement over the TMS-I procedure, this approach was abandoned.

In an attempt to overcome the problem of the hydrogenation byproduct of the *p*-NO_2-CBZ derivative, the unsubstituted benzyl carbamate (CBZ) was prepared. In this system the hydrogenation byproduct is toluene and the resultant Cp*Ru(η^6-trypt)OTf (**3**) can then easily be purified under vacuum. Initially it was feared that the N_b-CBZ tryptamine **15** might not exhibit chemospecific coordination of the Cp*Ru$^+$ moiety at indole due to competing η^6 coordination at the *O*-benzyl substituent. Treatment of **15** with 1 equiv of **1** under standard reaction conditions led to chemospecific coordination of the Cp*Ru$^+$ moiety at the indole carbocyclic ring. This provided Cp*Ru(η^6-N_b-CBZ-trypt)OTf (**16**) as an oil in 97% isolated yield.

To date, attempts to crystallize the complex **16** have been unsuccessful. As a result, we have found it easier to handle the material as a solid foam. The foam is generated by dissolving the oil in dry dichloromethane and removing

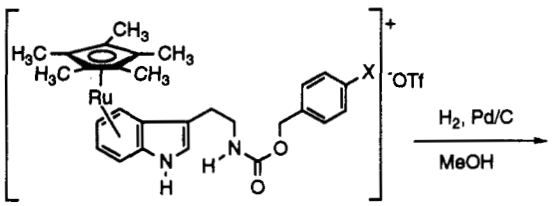
(13) For a review of the Pictet–Spengler reaction see: Ungemach, F.; Cook, J. M. *Heterocycles* **1978**, *9*, 1089.
(14) Lott, R. S.; Chauhan, U. S.; Slammer, C. H. *J. Chem. Soc., Chem. Commun.* **1979**, 495.
(15) Exner, O. In *Correlation Analysis in Chemistry: Recent Advances*; Chapman, N.B., Shorter, J., Eds.; Plenum Press: New York, 1978; p 439, and references cited therein.
(16) Vichard, D.; Grusselle, M.; Amouri, H.; Jaouen, G.; Vaissermann, J. *Organometallics* **1992**, *11*, 2952.

Table 2. Cp*R(η^6-CBZ-trypt)OTf Derivatives[a]

N_b-CBZ-trypt	Cp*Ru(η^6-N_b-trypt)OTf	yield, %[b]
 **13**	 **14**	91
 **15**	 **16**	97
 **17**	 **18**	92
 **19**	 **20**	94
 **21**	 **22**	90

[a] All compounds were prepared using the general procedure described in the Experimental Section. [b] Isolated yields of purified compounds.

Scheme 3



14 X = NO_2
16 X = H

3

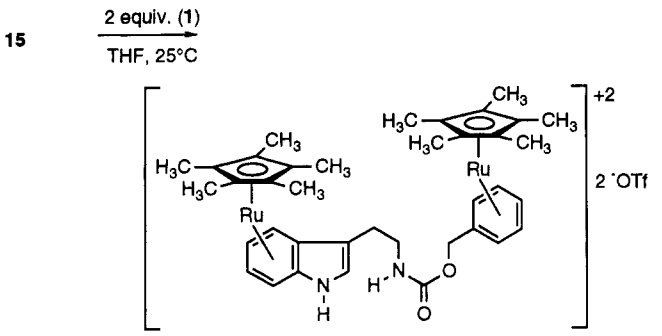
the solvent under reduced pressure. This results in the inclusion of one molecule of dichloromethane per molecule of complex as observed by NMR and microanalysis. In this form the complex **16** is an air-stable, free flowing solid which can be easily handled or stored; however, in this form the compound is still very hygroscopic and appropriate precautions must be taken.[12]

With the benzyloxy derivative **16** in hand, deprotection of the benzyloxy carbamate was attempted. Hydrogenolysis of **16** under anhydrous conditions (10% Pd/C, H_2, CH_3OH) afforded the Cp*Ru(η^6-trypt)OTf (**3**) in 87% isolated yield (Scheme 3) in a high degree of purity as determined by NMR.[17] This procedure greatly enhanced the synthetic potential of **3** for the preparation of substituted tryptamine and tryptamine-related compounds. To date, the synthesis of **3** has been carried out easily on a 1-mmol scale to furnish synthetically useful quantities of Cp*Ru(η^6-trypt)OTf (**3**). In addition, the CBZ protecting group strategy was found to be ideally suited for the preparation of a variety of Cp*Ru(η^6-trypt)-OTf derivatives. This chemistry has been readily extended to several other tryptamine-related systems, resulting in the syntheses of both the tryptamine complex **18** and the β-carboline (β-carb) complex **20** in high yields (Table 2).

The chemospecificity observed in the syntheses of compounds **8**, **14**, **16**, **18**, and **20** is quite striking and further illustrates the sensitivity of the Cp^*Ru^+ moiety generated from Cp*Ru(CH_3CN)$_3$OTf (**1**) to the electronic nature of arenes.[16,18] Given the nature of the reaction conditions, the observed chemospecificity is probably governed by the kinetic effects inherent to η^6 coordination of the Cp^*Ru^+ moiety. Mann *et al.* have demonstrated that the kinetically controlled η^6 coordination of the Cp^*Ru^+ moiety favors arene π systems which are partially localized over arene π systems which are highly delocalized.[18] Therefore, in these systems the kinetics of η^6 coordination of Cp^*Ru^+ would favor the indole π system over the highly delocalized

(17) ^1H and ^{13}C NMR spectra are available as supplementary material.
(18) Koefod, R. S.; Mann, K. R. *J. Am. Chem. Soc.* **1990**, *112*, 7287.

Scheme 4



23 (55% yield)

aromatic π system of the substituted phenyl ring of the CBZ group. The electron-rich π-system of the indole not only is more attractive to the electrophilic Cp*Ru$^+$ moiety but also can stabilize a η^2 precoordination intermediate better than the less electron rich delocalized arenes of the CBZ group. It is interesting to note that the kinetically controlled chemospecificity observed in these systems is in complete agreement with thermodynamic trends measured for the η^6 arene coordination of Cp*Ru(CH$_3$CN)$_3$OTf (1).[9] Therefore, the observed products are not only kinetically favored but also thermodynamically favored. This is consistent with the fact that even when the reactions were performed at high temperature (boiling THF) over extended reaction times no intramolecular migration of the Cp*Ru$^+$ moiety from the indole to the phenyl ring was observed.

In order to demonstrate that the observed kinetically derived chemospecificity is due to the nature of π delocalization of indole and not the electron density of the arenes, the *p*-CH$_3$O-CBZ tryptamine **21** was prepared. Although the *p*-CH$_3$O-CBZ unit is an electron-rich moiety (σ_p = −0.28),[15] on the basis of the kinetic arguments of π localization, chemospecific η^6 coordination to the indole ring was expected. The reaction of **21** with **1** under standard conditions yielded the expected Cp*Ru(η^6-N_b-(*p*-MeO-CBZ)-trypt]OTf (**22**), exclusively, in 92% yield (Table 2). In this example the Cp*Ru$^+$ unit differentiates between two electron-rich arenes, favoring the indole nucleus over the highly delocalized aromatic phenyl ring, in a chemospecific fashion. Moreover, attempts to isomerize the complex **22** in boiling THF were unsuccessful, thus further demonstrating that the thermodynamics of the system are in agreement with trends measured in isolated arene systems.[9]

Binuclear Organoruthenium Complexes. It was of general interest to explore the possibility of preparing a binuclear Cp*Ru complex.[19] Formation of a binuclear complex would further demonstrate that the chemospecificity observed in these tryptamine systems is directed by the kinetic coordination of Cp*Ru$^+$ and is not necessarily a function of the thermodynamic stability of the Cp*Ru(η^6-substituted-CBZ)OTf complex. The synthesis of the binuclear complex **23** was achieved by treatment of **15** with 2 equiv of **1** in a stirred solution of THF at 25 °C, under an atmosphere of argon. This afforded [Cp*Ru-(η^6-N_b-CBZ)-Cp*Ru(η^6-trypt)](OTf)$_2$ (**23**) as a microcrystalline solid in 55% isolated yield (Scheme 4). The binuclear Cp*Ru complex **23** was found to be an air stable solid, the structure of which was confirmed by two-dimensional ^{1}H–^{1}H COSY NMR and microanalysis. This clearly demonstrates that η^6 coordination of Cp*Ru$^+$ to the phenyl ring of the CBZ group does provide a stable complex. However, it was not surprising to find that treatment of the benzamide compound **7** and *p*-NO$_2$-CBZ species **13** with 2 equiv of **1** did not yield stable binuclear Cp*Ru complexes. Presumably in these systems the electron-deficient aryl units of **7** and **13** form thermodynamically unstable Cp*Ru(η^6-substituted-CBZ)OTf complexes, which readily decompose under ambient reaction conditions.

Conclusions

In the polyaromatic tryptamine systems described above, the Cp*Ru moiety demonstrated remarkable chemospecificity for the partially localized π system of the indole nucleus in the presence of a variety of substituted arenes. This resulted in the kinetic formation of a single complex which also is the thermodynamically favored product. The chemospecificity of Cp*Ru$^+$ for the indole nucleus has been exploited synthetically for the preparation of the first transition metal η^6-tryptamine complex, Cp*Ru(η^6-trypt)OTf (**3**). Moreover, this approach has led to the synthesis of a variety of mono- and binuclear polyaromatic systems. The potential of this approach for the synthesis of biologically interesting Cp*Ru(η^6-arene)-OTf complexes[16,20] (alkaloids, biogenic amines, amino acids, and peptides) is quite promising and is the subject of current investigations.

Experimental Section

All syntheses were carried out in a glovebox equipped with a constant argon flush. Solvents were dried and distilled under nitrogen before use by employing the following drying agents: tetrahydrofuran (THF) (Na/K dispersion); CH$_3$CN (P$_2$O$_5$); CH$_3$OH (Mg); CD$_3$NO$_2$ (vacuum transferred from P$_2$O$_5$); CH$_2$Cl$_2$ (P$_2$O$_5$); Et$_2$O (Na/benzophenone). The reagent Cp*Ru(CH$_3$CN)$_3$OTf (**1**) was synthesized as previously reported.[21] All the amides and carbamates utilized in this study were prepared from tryptamine and corresponding acylating reagents, employing standard reaction conditions.[12] All chemicals and reagents not otherwise noted were purchased from Aldrich Chemical Co. Milwaukee, WI. NMR spectra were recorded using a Varian Gemini 300-MHz spectrometer. Analytically pure samples were obtained using reverse-phase HPLC chromatography on a Waters Semi-Prep HPLC system with NOVA-Pak C18 cartridges.

General Procedure. To a stirred solution of the N_b-acyltryptamine (0.2 mmol) in THF (10 mL) at room temperature under an argon atmosphere in a glovebox was added in one portion Cp*Ru(CH$_3$CN)$_3$OTf (**1**; 101 mg, 0.2 mmol). The reaction mixture was stirred for 2 h. The reaction mixture was removed from the glovebox, and the solvent was removed under reduced pressure. The immiscible oil was rinsed with anhydrous Et$_2$O (3 × 5 mL). This was done to remove any extraneous organic material and/or precipitate the complex. The oil or solid was then dried under high vacuum to afford the complex in pure form as determined by NMR.

(19) (a) Fagan, P. J.; Ward, M. P.; Casper, J. V.; Calabrese, J. C.; Kursic, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 2981. (b) Ward, M. D.; Fagan, P. J.; Calabrese, J. C.; Johnson, D. C. *J. Am. Chem. Soc.* **1989**, *11*, 1719.

(20) (a) Moriarty, R. M.; Ku, Y. Y.; Gill, U. S. *J. Chem. Soc., Chem. Commun.* **1987**, 1837. (b) *J. Organomet. Chem.* **1989**, *363*, 187. (c) Moriarty, R. M.; Ku, Y. Y.; Gill, U. S.; Gilardi, R.; Perrier, R. E.; McGlinchey, M. J. *Organometallics* **1989**, *8*, 960. (d) Jaouen, G.; Vessieres, A.; Top, S.; Ismail, A. A.; Butler, I. S. *J. Am. Chem. Soc.* **1985**, *107*, 4778.

(21) Fagan, P. J.; Ward, M. D.; Calabrese, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 1698.

Cp*Ru(η^6-N_b-Ac-trypt)OTf (6): general procedure (108 mg, 92%); ^{1}H NMR ($CDCl_3$) δ 10.47 (s, 1H), 7.49 (s, 1H), 6.96 (br s, 1H), 6.47, (d, J =3.6 Hz, 1H), 6.31 (d, J = 3.6 Hz, 1H), 5.31 (m, 2H), 3.45 (m, 2H), 2.79 (m, 2H), 1.95 (s, 3H), 1.64 (s, 15H); ^{13}C NMR ($CDCl_3$) δ 170.7, 132.8, 112.9, 109.9, 93.0, 84.6, 84.3, 79.7, 74.5, 39.9, 25.8, 23.1, 9.91. Anal. Calcd for $C_{23}H_{29}N_2O_4F_3SRu\cdot{}^1/_2H_2O$: C, 46.30; H, 5.03; N, 4.69. Found: C, 46.04; H, 4.92; N, 4.66.

Cp*Ru(η^6-N_b-Bz-trypt)OTf (8): general procedure (120 mg, 93%); mp 167–168 °C dec; ^{1}H NMR ($CDCl_3$) δ 10.30 (s, 1H), 7.85 (d, 2H, J = 8.0 Hz), 7.68 (s, 1H), 7.46 (s, 1H), 7.38 (m, 3H), 6.42 (d, 1H, J = 5.2 Hz), 6.37 (d, 1H, J = 5.0 Hz), 5.28 (m, 2H), 3.66 (m, 2H), 2.92 (m, 2H), 1.62 (s, 15H); ^{13}C NMR ($CDCl_3$) δ 167.9, 134.1, 131.7, 128.5, 127.2, 111.7, 108.9, 96.1, 92.2, 82.9, 82.1, 78.1, 73.3, 40.0, 24.9, 9.6. Anal. Calcd for $C_{28}H_{31}N_2O_4F_3SRu\cdot H_2O$: C, 50.37; H, 4.98; N, 4.20. Found: C, 50.62; H, 4.72; N, 4.20.

Cp*Ru(η^6-N_b-BOC-trypt)OTf (10): general procedure (123 mg, 95%); ^{1}H NMR ($CDCl_3$) δ 7.42 (s, 1H, 2-H), 6.68 (d, J = 4.4 Hz, 1H), 6.38 (d, J = 4.5 Hz, 1H), 5.59 (m, 2H), 5.37 (br s, 1H), 3.43 (m, 2H), 2.88 (m, 2H), 1.66 (s, 15H), 1.41 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 156.1, 132.1, 111.0, 109.1, 96.1, 92.1, 83.0, 82.6, 79.5, 77.8, 73.8, 40.5, 28.4, 25.5, 9.7. Anal. Calcd for $C_{26}H_{35}N_2O_5F_3SRu$: C, 48.36; H, 5.46; N, 4.34. Found: C, 47.93; H, 5.45; N, 4.29.

Cp*Ru[η^6-N_a-(*i*-Pr_3Si)-N_b-BOC-trypt]OTf (12): general procedure (154 mg, 96%); ^{1}H NMR ($CDCl_3$) δ 10.57 (s, 1H), 7.52 (s, 1H), 6.67 (d, J = 4.5 Hz, 1H), 6.18 (d, J = 4.9 Hz, 1H), 5.33 (m, 2H), 4.89 (br s, 1H), 3.30 (m, 2H), 2.76 (t, J = 6.6 Hz), 1.73 (s, 15H), 1.41 (s, 9H), 1.16 (d, J = 7.5 Hz, 6H), 1.05 (d, J = 7.5 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 156.2, 136.8, 117.0, 116.2, 96.6, 92.9, 83.7, 78.9, 40.4, 28.4, 25.6, 18.2, 18.1, 17.8, 12.7. Anal. Calcd for $C_{35}H_{55}N_2O_5F_3SSiRu$: C, 52.41; H, 6.91; N, 3.49. Found: C, 52.35; H, 7.00; N, 3.50.

Cp*Ru[η^6-N_b-(*p*-NO_2-CBZ)-trypt]OTf (14): general procedure (135 mg, 91%); ^{1}H NMR ($CDCl_3$) δ 10.72 (s, 1H), 8.14 (d, J = 8.6 Hz, 2H), 7.56 (s, 1H), 7.50 (d, J = 8.3 Hz, 2H), 6.68 (d, J = 5.8 Hz, 1H), 6.09 (d, J = 5.5 Hz, 1H), 5.34 (t, J = 5.6 Hz, 1H), 5.29 (t, J = 5.5 Hz, 1H), 3.95 (s, 2H), 2.97 (m, 2H), 2.83 (m, 2H), 1.66 (s, 15 H); ^{13}C NMR ($CDCl_3$) δ 146.9, 131.8, 128.7, 128.6, 123.4, 111.7, 108.9, 95.9, 92.1, 82.9, 82.6, 77.7, 73.5, 65.8, 52.8, 48.9, 25.1, 9.5. Anal. Calcd for $C_{29}H_{32}N_3O_7F_3SRu$: C, 48.06, H, 4.45; N, 5.80. Found: C, 47.83; H, 4.80; N, 5.88.

Cp*Ru(η^6-N_b-CBZ-trypt)OTf (16).[17] To a stirred solution of **15** (306 mg, 1 mmol) in THF (50 mL) at room temperature under an argon atmosphere was added in one portion Cp*Ru-($CH_3CN)_3$OTf (1; 508 mg, 1.0 mmol). The reaction mixture was stirred for 30 min. It was then removed from the glovebox, and the solvent was removed under reduced pressure. The immiscible oil was rinsed with anhydrous Et_2O (3 × 5 mL) to remove any extraneous organic material. The oil was dissolved in CH_2Cl_2 (10 mL), and the solvent was removed under reduced pressure. This gave a solid foam which was further dried under high vacuum for 3 h to furnish **16** in pure form (740 mg, 97%): ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 7.45 (s, 1H), 7.31 (s, 5H), 6.55 (d, 1H, J = 5.7 Hz), 6.20 (d, 1H, J = 5.5 Hz), 5.46 (br s, 1H), 5.27 (m, 2H), 5.07 (d, J = 3.2 Hz, 2H), 3.40 (m, 2H), 2.78 (m, 2H), 1.63 (s, 15H); ^{13}C NMR ($CDCl_3$) δ 156.9, 136.6, 131.9, 128.5, 127.9, 111.0, 109.1, 96.1, 92.5, 82.9, 82.6, 77.3, 73.6, 66.5, 40.9, 25.3, 9.6. Anal. Calcd for $C_{29}H_{33}N_2O_5F_3SRu\cdot CH_2Cl_2$: C, 47.12, H, 4.61; N, 2.26. Found: C, 47.43; H, 4.80; N, 2.18.

Cp*Ru(η^6-N_b-CBZ-5-$PhCH_2O$-trypt)OTf (18): general procedure (144 mg, 92%); ^{1}H NMR ($CDCl_3$) δ 10.86 (s, 1H), 7.38–7.25 (m, 11H), 6.63 (d, J = 5.2 Hz, 1H), 6.27 (s, 1H), 5.37 (d, J = 5.1 Hz, 1H), 5.20 (s, 1H), 5.01 (s, 2H), 4.91 (s, 2H), 3.43 (m, 2H), 2.78 (m, 2H), 1.65 (s, 15 H); ^{13}C NMR ($CDCl_3$) δ 156.4, 136.4, 134.7, 128.8, 128.4, 127.8, 127.6, 110.5, 107.4, 95.2, 91.8, 73.5, 71.9, 77.7, 67.2, 66.7, 41.1, 25.6, 9.8. Anal. Calcd for $C_{36}H_{39}N_2O_6F_3SRu$: C, 55.02, H, 5.00; N, 3.56. Found: C, 54.78; H, 4.69; N, 3.18.

Cp*Ru(η^6-N_b-CBZ-1,2,3,4-H_4-β-carb)OTf (20): general procedure (125 mg, 94%); ^{1}H NMR ($CDCl_3$) δ 10.7 (s, 1H), 7.37 (m, 5H), 6.61 (d, J = 5.1 Hz, , 1H), 5.96 (d, J = 4.9 Hz, 1H), 5.34 (m, 2H), 5.18 (s, 2H), 4.78 (d, J_{AB} = 15 Hz, 1H), 4.63 (d, J_{AB} = 15 Hz, 1H), 3.88 (m, 1H), 3.70 (m, 1H), 2.68 (m, 2H), 1.66 (s, 15 H); ^{13}C NMR ($CDCl_3$) δ 155.3, 142.0, 136.2, 128.4, 127.9, 127.6, 110.5, 108.6, 95.0, 92.4, 82.7, 73.8, 67.5, 42.3, 42.0, 21.6, 9.9. Anal. Calcd for $C_{30}H_{33}N_2O_5F_3SRu\cdot H_2O$: C, 50.77; H, 4.97; N, 3.95. Found: C, 50.40; H, 4.83; N, 3.95.

Cp*Ru[η^6-N_b-(*p*-CH_3O-CBZ)-trypt]OTf (22): general procedure (127 mg, 90%); ^{1}H NMR ($CDCl_3$) δ 10.5 (s, 1H), 7.48 (s, 1H), 7.27 (d, J = 7.2 Hz, 2H), 6.87 (d, J = 7.3 Hz, 2H), 6.61 (d, J = 5.4 Hz, 1H), 6.17 (d, J = 4.9 Hz, 1H), 5.30 (m, 2H), 5.02 (s, 2H), 3.80 (s, 3H), 2.78 (m, 2H), 1.65 (s, 15 H); ^{13}C NMR ($CDCl_3$) δ 159.4, 132.1, 129.9, 128.5, 122.9, 118.4, 113.9, 110.8, 109.1, 96.1, 92.2, 82.9, 76.2, 73.8, 55.4, 41.1, 25.4, 9.8. Anal. Calcd for $C_{30}H_{33}N_2O_5F_3SRu\cdot{}^1/_2CH_2Cl_2$: C, 48.65; H, 4.82; N, 3.72. Found: C, 48.44; H, 4.79; N, 3.83.

[Cp*Ru(η^6-N_b-CBZ)-Cp*Ru(η^6-trypt)](OTf)$_2$ (23). To a stirred solution of **15** (27 mg, 0.1 mmol) in THF (5 mL) at room temperature under an argon atmosphere was added in one portion Cp*Ru($CH_3CN)_3$OTf (1; 101 mg, 0.2 mmol). The reaction mixture was stirred for 18 h. It was then removed from the glovebox, and Et_2O was added to afford **23** as a microcrystalline solid. The solvent was removed via micropipet; the crystalline material was washed with Et_2O (2 × 5 mL) and dried under high vacuum to furnish the bis-Cp*Ru complex **23** (54 mg, 55%): mp 174–175 °C dec; ^{1}H NMR ($CDCl_3$) δ 10.37 (s, 1H), 7.55 (s, 1H), 6.87 (s, 1H), 6.59 (d, 1H, J = 5.1 Hz), 6.38 (d, 1H, J = 5.3 Hz), 5.90 (m, 2H), 5.76 (m, 2H), 5.66 (m, 1H), 5.42 (m, 2H), 4.80 (s, 2H), 3.49 (m, 2H), 2.88 (m, 2H), 1.94 (s, 15H), 1.66 (s, 15H). Anal. Calcd for $C_{40}H_{48}N_2O_8F_6S_2Ru_2$: C, 45.11; H, 4.55; N, 2.63. Found: C, 44.60; H, 4.53; N, 2.79.

Hydrogenolysis of 16. Synthesis of Cp*Ru(η^6-tryptamine)OTf (3).[17] A solution of **16** (200 mg, 0.26 mmol) in dry CH_3OH (5 mL) and 10% Pd/C (20 mg) were stirred under a hydrogen atmosphere (1 atm) for 24 h. The catalyst was removed by filtration through a pad of Celite. The filter cake was washed with dry CH_3OH (2 × 10 mL), and the filtrate was concentrated under reduced pressure to furnish **3** as an oil (123 mg, 87%): ^{1}H NMR (CD_3OD) δ 7.89 (s, 1H), 7.65 (s, 1H), 6.44 (d, J = 5.5 Hz, 1H), 6.34 (d, J = 5.7 Hz, 1H), 5.58 (m, 2H), 3.01 (m, 2H), 2.85 (m, 2H), 1.71 (s, 15H); ^{13}C (CD_3OD) δ 134.5, 110.2, 110.1, 96.8, 94.2, 85.2, 85.1, 84.6, 79.2, 74.6, 41.0, 23.8, 9.92.

Deprotection of 10. Alternative Synthesis of 3. To a stirred solution of **10** (290 mg, 0.46 mmol) and sodium iodide (74 mg, 0.50 mmol) in acetonitrile (15 mL) at room temperature was added trimethylsilyl chloride (62 μL, 0.50 mmol). The reaction mixture was stirred under a nitrogen atmosphere for 12 h. It was then filtered and the solvent removed under reduced pressure. The resultant oil was dissolved in CH_2Cl_2 and filtered again. The filtrate was concentrated, and diethyl ether (5 mL) was added to the residue. The ethereal solution was separated from the insoluble oil with a micropipet. The ethereal wash was repeated twice, and the oil was dried under vacuum to afford **3** (149 mg, 61%).

Acknowledgment. We wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society (PRF-ACS), and the National Science Foundation for the financial support of this research. The Louisiana Board of Regents is acknowledged for allocating funds for the purchase of NMR spectrometers (Grant No. ENH-53, 1990–1991). We also gratefully acknowledge the Johnson-Matthey/Aesan Co. for their generous loan of ruthenium salts.

Supplementary Material Available: Figures giving ^{1}H and ^{13}C NMR spectra for compounds **3** and **16** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the American Chemical Society. Ordering information is given on any current masthead page.

OM930652E