Synthesis and Nucleophilic Displacement Reactions of Novel (η^6-4-,5-, or 7-Nitro-*N*-methylindole)(η^5-cyclopentadienyl)ruthenium Hexafluorophosphates

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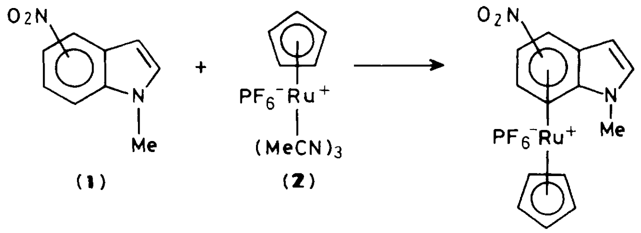
Novel cyclopentadienylruthenium complexes of nitroindoles were synthesized *via* direct thermal ligand exchange using [Ru(C_5H_5)(MeCN)$_3$]PF_6 and they undergo smooth nucleophilic substitution with a range of oxygen, nitrogen, and carbon nucleophiles leading after decomplexation to indole derivatives.

Recently we reported a new method for substitution upon the halogenoindole nucleus by temporary co-ordination of the cyclopentadienylruthenium (CpRu) unit onto the aryl ring of indole. The strong electron withdrawing effect of the CpRu$^+$ unit activates the ring halogen towards nucleophilic displacement.[1,2] This strategy using CpFe$^+$ or CpRu$^+$ has been applied to nucleophilic displacement upon simple aromatic systems[3—5] and our work extended this approach to the indole system.[1,2]

Ring-substituted indoles are prevalent among natural product chemistry[6] and the goal of introduction of functional groups onto the aryl ring of indole nucleus led us to apply the temporary complexation method to the nitroindole system. We report now the first examples of ruthenium complexes of nitroindole derivatives and the nucleophilic substitution reactions of these novel complexes with various nucleophiles.

The nitro group in nitroarenes can be activated towards nucleophilic displacement by other electron-withdrawing substituents such as a second nitro group.[7—9] The ready nucleophilic displacement of a chlorine atom in CpRu$^+$ complexes is well established.[1,2,10] The analogous displacement of the nitro group has not been reported and the failure to achieve direct complexation of nitroarene may account for this lacuna.

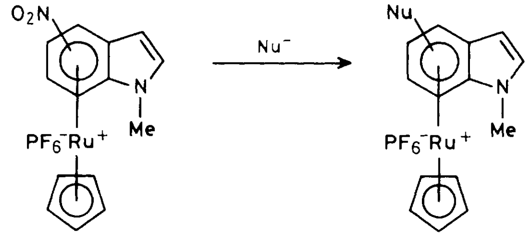
Direct incorporation of the cyclopentadienylruthenium unit onto the rather electron deficient aryl ring of the nitroindole system by the direct ligand exchange reaction of cyclopentadienyltrisacetonitrileruthenium was achieved for 4-, 5-, and 7-nitroindoles as follows (Scheme 1): under nitrogen, a mixture of (**1a**, **b**, or **c**) (1.3 mmol) and the salt (**2**) (1.0 mmol)[10] in 1,2-dichloromethane was heated overnight at 40 °C. The solvent was removed *in vacuo* and the residue was



(**1**) (**2**) (**3**)

a; 4-NO_2
b; 5-NO_2
c; 7-NO_2

Scheme 1



(**3**) (**4**)-(**8**)

Scheme 2

Product	Nu	% Yield a (4-NO_2)	 b (5-NO_2)	 c (7-NO_2)
(**4**)	CH(CO_2Me)$_2$	84	88	76
(**5**)	CH(CO_2Et)$_2$	80	84	73
(**6**)	OMe	85	89	83
(**7**)	*N*-pyrrolidinyl	76	75	70
(**8**)	*N*-piperidyl	75	72	67

washed with ether; the solid was crystallized from acetone/ether to give the corresponding 4-, 5-, and 7-nitro-*N*-methylindole complexes (**3a**—**c**) in 50—60% yields [based on the salt (**2**)].

The structural assignments of these new nitroindole cyclopentadienylruthenium complexes are based on high resolution ^{1}H n.m.r., ^{13}C n.m.r., and analytical data. The ^{1}H n.m.r. spectra were especially informative and display the characteristic upfield shift for the protons at the aryl ring bound to the ruthenium metal unit, which is very similar to our observation in chloroindole series.[2]

Complexes (**3a**—**c**) were found to undergo smooth nucleophilic substitution of the nitro group with a range of carbon, oxygen, and nitrogen nucleophiles leading to the formation of substituted indoles (Scheme 2). The structures are based upon ^{1}H n.m.r., ^{13}C n.m.r., and microanalytical data. Typically, using carbanions derived from dimethyl or diethyl malonate as nucleophiles, complexes (**3a**—**c**) underwent exclusive *ipso*-displacement of the nitro group. The reactions were carried out as follows. A mixture of the complex (**3a**, **b**, or **c**) (1.0 mmol), K_2CO_3 (2.5 mmol), and the malonate (2.0 mmol) in 20 ml of tetrahydrofuran (THF) was refluxed for 6 h under nitrogen and filtered rapidly into a flask containing 10% HCl (10 ml); after the standard work up,[3a] the corresponding products (**4**)—(**8**) were obtained in high yields.†

It is noteworthy that the sterically hindered nitro group of the 7-nitro-*N*-methylindole ruthenium complex was displaced readily by various nucleophiles.

These results indicate the feasibility of using the cyclopentadienylruthenium unit as an auxiliary to activate the nitro group displacement with oxygen, nitrogen, and carbon nucleophiles. The commercial availability of nitroindole makes the ruthenium complexes of nitroindole excellent substrates for regiospecific functionalization of the indole nucleus. Disengagement of the cyclopentadienylruthenium unit was accomplished either by high vacuum sublimation or by photolysis in MeCN. A significant feature of the latter method is that $[(MeCN)_3Ru(Cp)]PF_6$ can be regenerated and recycled.

In conclusion, this work represents the first examples of cyclopentadienylruthenium complexes of nitroindole derivatives and indicates that the $CpRu^+$ unit provides strong activation for nitro group displacement, and concomitantly, for selective functionalization of the indole nucleus.

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† All new ruthenium complexes were characterized, *inter alia*, by ^{1}H n.m.r., ^{13}C n.m.r., and satisfactory combustion analysis (C, H). Selective data are as follows: (**3c**): ^{1}H n.m.r. [400 MHz, $(CD_3)_2CO$] δ 7.97 (d, 1H), 7.28 (d, 1H), 6.91 (d, 1H), 6.96 (d, 1H), 6.33 (t, 1H), 5.32 (s, 5H), and 3.90 (s, 3H); ^{13}C n.m.r. [400 MHz, $(CD_3)_2CO$] δ 144.97, 106.23, 105.75, 105.39, 97.41, 82.55, 81.87, 81.36, 79.38, and 36.69. (**4a**): ^{1}H n.m.r. [400 MHz, $(CD_3)_2CO$] δ 7.80 (d, 1H), 7.14 (d, 1H), 6.69 (d, 1H), 6.14 (d, 1H), 6.05 (t, 1H), 5.41 (s, 1H), 4.99 (s, 5H), 3.92 (s, 3H), 3.82 (s, 3H), and 3.77 (s, 3H); ^{13}C n.m.r. [400 MHz, $(CD_3)_2CO$] δ, 167.79, 167.62, 142.49, 101.88, 110.52, 98.39, 89.57, 82.36, 81.11, 70.29, 79.98, 54.56, 53.72, and 33.52. (**7b**): ^{1}H n.m.r. [400 MHz, $(CD_3)_2CO$] δ 7.60 (d, 1H), 6.83 (d, 1H), 6.54 (d, 1H), 6.41 (d, 1H), 5.51 (d,d, 1H), 4.97 (s, 5H), 3.73 (s, 3H), 3.23 (m, 4H), 1.99 (m, 4H), ^{13}C n.m.r. [400 MHz, $(CD_3)_2CO$] δ 141.46, 121.48, 107.85, 103.68, 95.89, 77.40, 67.12, 65.89, 62.77, 49.29, 33.24, and 25.37.