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Preliminary Communication

Synthesis and reactivity of (indole)Mn(CO)$_3$$^+$ complexes. Electrophilic activation of the indole 4 and 7 positions

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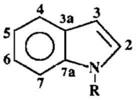
Due to the importance of the indole nucleus **1** as the basic structural unit in many natural products, an enormous amount of research has dealt with the functionalization of the pyrrole and the carbocyclic rings [1]. While electrophilic substitution at the electron-rich pyrrole C-2 and C-3 positions is easily achieved, functionalization at the carbocyclic C-4 and C-7 positions is difficult. Recently, progress in this regard has been made using organometallic reagents [2–6]. Nucleophilic substitution of the chloride in 4- and 5-chloroindoles is facilitated by complexation of the carbocyclic ring to the CpRu$^+$ moiety [3]. Electrophilic activation of the C-4 and C-7 positions in (indole)Cr(CO)$_3$ complexes is great enough to permit attack by strong carbanion donors; the preference for C-4 or C-7 attack can be modulated by placing substituents with suitable electron/steric properties at C-3 or N-1 [4, 5]. In a related approach, lithiation of the C-4 or C-7 sites in (indole)Cr(CO)$_3$ complexes, followed by treatment with an electrophile, affords substitution at these positions [6].

It is known that arenes can be coordinated under mild conditions to the Mn(CO)$_3$$^+$ moiety and that the resultant (arene)Mn(CO)$_3$$^+$ complexes are very electrophilic [7, 8]. Reaction with a wide range of nucleophiles, including weak ones, can be used as a means of introducing functionalities on the arene; some recent applications of biological interest are given in ref. 9. Indoles deprotonated at the nitrogen are known to coordinate to Mn(CO)$_3$$^+$ through the pyrrolyl ring to afford η^5-indolyl complexes [10]. We report herein that free indoles containing hydrogen or other substituents at the nitrogen bind to the metal through the carbocyclic ring to form (indole)Mn(CO)$_3$$^+$ complexes that are highly electrophilic at C-4 and C-7, thus providing a route to the direct functionalization of the indole nucleus at these positions. In comparison to chromium and ruthenium analogues (*vide supra*), the manganese systems may prove to be especially useful due to superior [8] electrophilic activation.

The indole complexes **2** were prepared as BF$_4$$^-$ salts by stirring Mn(CO)$_5$Br in CH$_2$Cl$_2$ with one equivalent of AgBF$_4$ for 1 h, then adding a slight excess of the indole and refluxing for 1 h. After filtration, the solvent was removed and the residue extracted with acetone. The products were precipitated with diethyl ether in yields of 60 to 90%. Five indole complexes were synthesized in this manner (**2**: R = H, Me, tosyl, SiPh$_2$Bu^t, SiPr^i$_3$). The benzofuran analogue **3** was similarly synthesized in 60% yield. All new complexes were characterized by NMR and IR. For example, for [(indole)Mn(CO)$_3$]BF$_4$ (**2**, R = H): IR (CH$_2$Cl$_2$): 2069, 2008 cm^{-1}; ^{1}H NMR (CD$_3$COCD$_3$): δ 11.6 (s, N–H), 8.24 (d, J = 3.2, H^2), 7.76 (d, J = 7, H^7), 7.60 (d, J = 7, H^4), 6.99 (d, J = 3.2, H^3), 6.60 (t, J = 6.5, H^5), 6.37 (t, J = 6.5, H^6); ^{13}C{^{1}H} NMR (CD$_2$Cl$_2$): δ 88.3 (C^7), 89.9 (C^5), 93.1 (C^6), 95.4 (C^4), 103.7 (C^{3a}), 104.8 (C^3), 117.2 (C^{7a}), 140.3 (C^2). *Anal.* Calc. for C$_{11}$H$_7$NO$_3$MnBF$_4$: C, 38.5; H, 2.06; N, 4.08. Found: C, 38.4; H, 2.01; N, 4.03%. For [(benzofuran)Mn(CO)$_3$]BF$_4$ (**3**): IR (CH$_2$Cl$_2$): 2080, 2019 cm^{-1}; ^{1}H NMR (CD$_3$NO$_2$): δ 8.31 (d, J = 2, H^2), 7.47 (d, J = 7, H^4), 7.38 (d, J = 7, H^7), 7.27 (d, J = 2, H^3), 6.61 (t, J = 6.5, H^6), 6.32 (t, J = 6.5, H^5); FAB-MS, *m/z* 257 (M^+).



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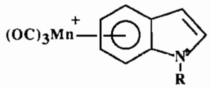

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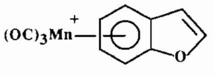

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Verification that the manganese in **2** is coordinated to the carbocyclic and not the pyrrole ring was provided by the X-ray structure of **2** (R = H), shown in Fig. 1**.

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**Crystal data for [(indole)Mn(CO)$_3$]BF$_4$: space group $P2_1/c$ with a = 10.026(2), b = 10.202(3), c = 13.480(4) Å, β = 102.06(2)°, V = 1348.4(6) Å^3, Z = 4, D_{calc} = 1.69 g cm^{-3}. Data collected at 20 °C on a Nicolet R3m diffractometer with Mo Kα radiation, μ = 9.92 cm^{-1}, 2θ scan limits 4.0–50°, 222 variables refined with 2087 unique reflections $I > 1.0\sigma(I)$ to R = 0.059 (R_w = 0.061, GOF = 1.79).

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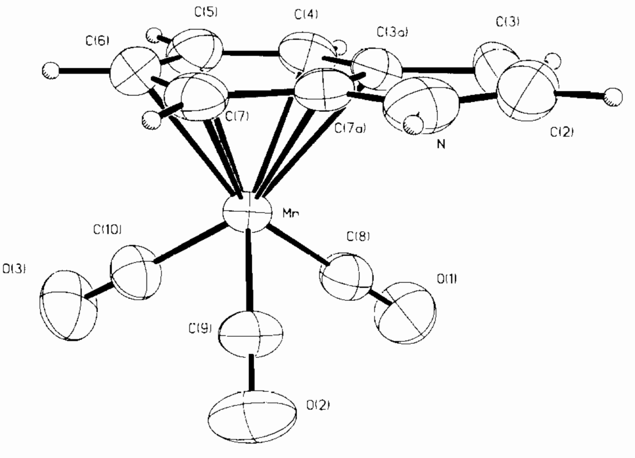


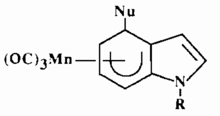
Fig. 1. An ORTEP drawing of the cation in $[(\text{indole})Mn(CO)_3]BF_4$ with the thermal ellipsoids at the 50% level.

TABLE 1. Results of nucleophilic addition to indole and benzofuran complexes **2** and **3**[a]

Complex	Nucleophile	Yield[b] (%)	Product ratio[c] C-4/C-7
2, R=H	$NaBH_4$	86	0.8
2, R=Me	$NaBH_4$	85	0.5
2, R=Me	LiMe	68	0.5
2, R=Me	$LiCMe_2CN$	68	2
2, R=Me	$LiCH_2CO_2Bu^t$	70	0.7
2, R=Me	$NaCH(CO_2Me)_2$	[d]	3
2, R=tosyl	LiMe	66	1
2, R=tosyl	$LiCMe_2CN$	65	2
2, R=$SiPh_2Bu^t$	$LiCMe_2CN$	70	5
2, R=$SiPr^i_3$	$LiCMe_2CN$	30[e]	>10
3	Bu_4NBH_4	70	2
3	LiMe	80	1.2

[a] Reactions were done in THF or CH_2Cl_2 at room temperature for BH_4^- additions and at −78 °C for all other nucleophiles. [b] Isolated yield consisting of a mixture of complexes **4** and **5**. [c] This is the ratio of **4** to **5**. [d] Product not isolated; yield >90% by IR. [e] Yield of desilylated product; see text.

The molecule has a 'piano stool' structure with a planar indole ligand and with highly linear Mn–C–O linkages that almost exactly bisect the carbocyclic bonds C(3a)–C(4), C(5)–C(6) and C(7)–C(7a). The average Mn–indole bond length is 2.216(5) Å, but there exists considerable variation; the bonds to the bridgehead carbons C(3a) and C(7a) are the longest at 2.293(5) and 2.290(4) Å, next in length are C(4) and C(7) at 2.204(6) and 2.197(3) Å, and the shortest are C(5) and C(6) at 2.158(6) and 2.155(5) Å. $NaBH_4$ reacted rapidly with complex **2** (R=H) in THF to give an 86% isolated yield of the product of hydride addition to C-4 and C-7 (complexes **4** and **5**, ratio 0.8:1). Other nucleophiles, e.g. LiMe, NaH, $LiCH_2C(O)CMe_3$, did not add to the indole, but instead deprotonated the N–H.



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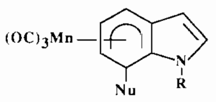

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Addition to the indole complexes having substituents other than R=H on the pyrrole nitrogen occurred at C-4 and/or C-7 for a range of nucleophiles, including ones as weak as $NaCH(CO_2Me)_2$. A summary of the results is given in Table 1*. (The benzofuran complex **3** also underwent nucleophilic attack at C-4 and C-7.) An examination of the C-4/C-7 product ratios indicates that it is possible to direct attack predominantly at the C-4 site provided the R group on the pyrrole nitrogen presents sufficient steric bulk. For example, with $LiCMe_2CN$ as the nucleophile, large silyl groups on the nitrogen lead to a large ($-SiPh_2Bu^t$) or exclusive ($-SiPr^i_3$) preference for attack at C-4.

^1H NMR was used to determine the relative amount of **4** and **5** in the (unseparated) product mixtures. In order to verify the assignments, one of the dienyl isomers was isolated as follows. $LiCMe_2CN$ addition to **2** (R=$SiPr^i_3$) gave a single isomer as judged by NMR. Rapid chromatography on alumina caused partial desilylation and led to the isolation of both desilylated (30% yield) and silylated product (the latter being completely converted to the former upon stirring in a suspension of alumina in ether for 30 min). Crystals of the desilylated complex were easily grown; the X-ray structure is shown in Fig. 2**. As expected, the structure corresponds to isomer **4**, with the nucleophile *exo* to the metal. Several features of the structure in Fig. 2 are noteworthy. The dienyl part of the carbocyclic ring is planar and forms an angle of 6.5° with the pyrrole plane. The saturated carbon C-4 is folded about the dienyl plane by an angle of 29.6°. This value is much smaller than the 40–43° found [11] with other cyclohexadienyl–manganese systems and undoubtedly reflects the influence of bonding between the dienyl and pyrrole π systems. Also indicative of this interaction

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*All of the dienyl complexes **4** and **5**, as well as those derived from nucleophilic addition to **3**, were characterized by NMR and IR. For example, for **4** (R=Me, Nu=H): IR (CH_2Cl_2): 1999, 1912 cm^{-1}; ^1H NMR (CD_2Cl_2): δ 6.87 (d, J=3, H^2), 6.28 (d, J=6, H^7), 5.78 (d, J=3, H^3), 4.94 (t, J=6, H^6), 3.52 (s, Me), 3.5 (H^4), 3.19 (t, J=6, H^5), 2.64 (d, J=14, H^{4-exo}). For **5** (R=Me, Nu=H): ^1H NMR (CD_2Cl_2): δ 6.72 (d, J=3, H^2), 6.34 (d, J=5.5, H^4), 5.96 (d, J=3, H^3), 4.96 (t, J=6, H^5), 3.7 (dd, J=5.5, 14, H^7), 3.49 (s, Me), 3.16 (t, J=6, H^6), 2.75 (d, J=14, H^{7-exo}).

Crystal data for **4 (R=H, Nu=CMe_2CN): space group $P\bar{1}$ with a=9.715(4), b=13.703(5), c=13.593(6) Å, α=61.20(3), β=76.56(3), γ=70.74(3)°, V=1491.0(10) Å^3, Z=4, D_{calc}=1.44 g cm^{-3}. Data collected at 20 °C on a Nicolet R3m diffractometer with Mo Kα radiation, μ=8.59 cm^{-1}, 2θ scan limits 4.0–48°, 379 variables refined with 4335 unique reflections $I>1.0\sigma(I)$ to R=0.046 (R=0.047, GOF=1.81).

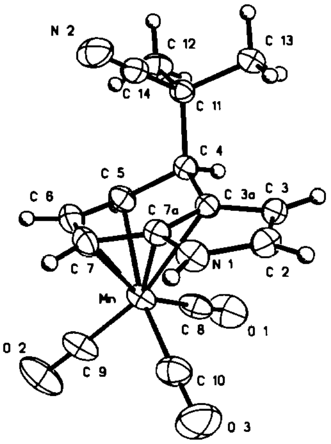

Fig. 2. An ORTEP drawing of complex **4** (R = H, Nu = CMe_2CN) with the thermal ellipsoids at the 30% level.

are long bond lengths between manganese and the bridgehead carbons; Mn–C(3a), 2.434(2); Mn–C(7a), 2.266(2) Å (compared to Mn–C(5), 2.162(3); Mn–C(6), 2.112(3) Å).

Supplementary material

Atomic numbering schemes and tables of crystallographic data, atomic positional parameters and thermal parameters, bond lengths and angles, and selected torsion angles for $[(indole)Mn(CO)_3]BF_4$ (**2**, R = H) and **4** (R = H, Nu = CMe_2CN) are available from the authors.

Acknowledgements

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