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Stereocontrolled Organomanganese Synthesis of *Cis*-4a,10b-Dihydrophenanthridine Derivatives

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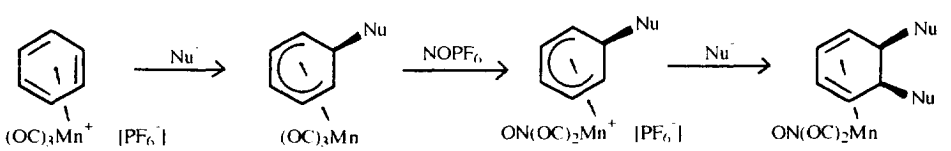
Abstract: *Cis-4a,10b-dihydrophenanthridine derivatives have been prepared in high yield via nucleophilic addition of a functionalised metalated arene to (benzene)tricarbonylmanganese(1+) hexafluorophosphate(1-) followed by reactivation, and intramolecular nucleophile addition.*

The regio- and stereocontrolled conversion of aromatic compounds into difunctionalised cyclohexadienes is a highly attractive process from a synthetic chemists viewpoint. Strategies to achieve this via double addition to transition metal arene complexes have had notable success with chromium[1] (5,6-*trans* difunctionalisation), and manganese[2] and iron[3] (5,6-*cis* difunctionalisation). The manganese approach, devised by Sweigart and Connelly[2b] involves initial nucleophile addition to a cationic arene complex [eg. (benzene)tricarbonylmanganese(1+) hexafluorophosphate(1-) (**1**)] to give a neutral cyclohexadienyl complex (**2**) (scheme 1). Subsequent reactivation by displacement of CO with NO^+ to give **3**, is followed by a second



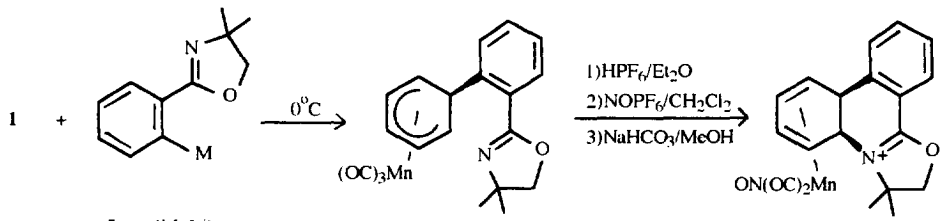
1 **2** **3** **4**

Scheme 1

nucleophile addition to give **4**. Although a wide range of nucleophiles react successfully in the first step, the range of nucleophiles known to react well in the second addition step has been limited mainly to hydride and phosphines.[5] We have aims to exploit this strategy by using an *ortho* functionalised metalated arene as the first nucleophile, and the *ortho* functional group as the second (intramolecular) nucleophile[4]. In this

communication, we demonstrate how this approach can eliminate the problem of poor nucleophile tolerance in the second addition step, and lead to some novel heterocyclic compounds which have high potential utility for natural product synthesis.

Carbon-carbon bond formation via addition of Li or grignard reagents to (arene)tricarbonylmanganese cations is by now a well established process. Although Li reagents are capable of giving CO attack in preference to ring attack[5], we have shown that in the case of metalloaryl reagents containing substituents *ortho* to the site of metalation, both types of reagent give good yields of ring coupled product upon reaction with **1**[4]. In a continuation of these studies, it was decided to investigate the reactivity of *ortho* metallophenyloxazoline derivatives **5a** and **5b** with **1** (scheme 2). Although the Li reagent gave a satisfactory



5a (M=Li)
b (M=MgBr)

6 **7**

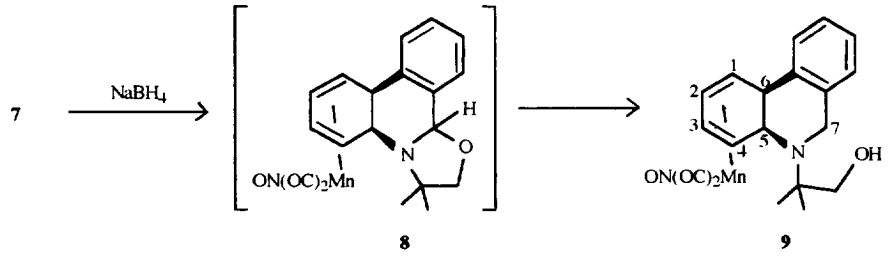
Scheme 2

yield (57%) of the expected 6-*exo*-substituted cyclohexadienyl product (**6**), the grignard reagent proved superior, giving a yield of 89%. This is consistent with other grignard additions to **1**, which have given yields from 80 to 90% [6]. Thus, although the Li reagent can be prepared from **5** (M=H)[7], and does not need the precursor bromo complex **5** (M=Br), the lower yield more than counteracts for this advantage. One contributory reason for the lower yield obtained from **5a** may be that *ortho* lithiophenyloxazoline compounds can undergo self condensation at 0°C.[7] In contrast, the grignard reagent **5b** is stable in refluxing THF[8].

Compound **6** was considered as a candidate for reaction with $NOPF_6$, however, under normal reaction conditions[2b], no evidence for the expected cationic product (**3**) was obtained. The failure of this reaction was readily attributable to the highly electrophilic NO^+ attacking the oxazoline nitrogen[9]. This problem was bypassed by initially protonating the N atom by dropwise addition of aqueous HPF_6 to an ethereal solution of **6**. The salt was filtered off, and reacted with $NOPF_6$ as a suspension in CH_2Cl_2 at R.T over 1 hour (scheme 2). Subsequent neutralisation allowed isolation of the desired cationic product in 72% yield. The product was observed to have structure **7**, in which the positive charge is located on N. Thus, the oxazoline N atom had undergone intramolecular nucleophilic addition to the cyclohexadienyl ring. The alternative structure (**3**) containing an unbound oxazoline group was discounted on the basis of spectroscopic data.[10] Furthermore, the H_5-H_6 coupling constant of 10 Hz, confirmed the *cis* stereochemistry.[2b,2c]

In order to assess the reactivity of this novel iminium ion, the reaction of **7** with $NaBH_4$ was carried out. It was expected that single H^- addition would occur at the iminium carbon to give compound **8**[11] (scheme 3), although an alternative pathway involving dissociation of the oxazoline nitrogen to afford a cyclohexadienyl structure (eg **3**) and H^- addition at the dienyl terminus (see scheme 1) was also considered

possible. However, spectroscopic analysis[10] clearly indicated that the single product (**9**) arose from a second addition of H^- to **8** resulting in cleavage of the oxazoline ring (scheme 3). When the reaction was carried out



8 **9**

Scheme 3

using greater than 2 equivalents of $NaBH_4$, the product was obtained cleanly in 97% yield, however, less than two equivalents resulted mainly in a mixture of compound **9** and starting material (**7**) as observed by TLC. This observation suggests that the cyclic hemiaminal moiety in **8** readily decomposes under reaction conditions to afford a second iminium ion which competes with **7** for addition of hydride. The two hydrogens on the newly created methylene centre, C7, which were observed in the ^1H NMR at 3.6 and 3.9 ppm exhibited a large geminal coupling constant of 16 Hz due to the adjacent aromatic π-system[12]. The two hydrogens H5 and H6 were again observed to have a large vicinal coupling constant of 10 Hz, reconfirming the *cis* stereochemistry.

Previously, nitrogen based nucleophiles have failed to afford the desired products upon reaction with complexes of type **3**[5b]. This observation suggests that it is the intramolecular nature of our approach which increases the probability of a successful addition. Thus, this method has provided a short and high yield route to the novel heterocyclic structures **7** and **9** in three steps from simple aromatic starting materials. Removal of the $Mn(CO)_2NO$ moiety from complexes of type **4** has been carried out successfully by Chung[5c] using amine oxides. We are now planning to investigate similar reactions for **7** and **9**, including alternative methods which may allow reclamation of the Mn group. Further functionalisation of the heterocyclic ring system is also a high priority. In this sense, the presence of the OH group on the side chain is an advantage as this may be useful for further cyclisation. Ultimately, we hope to be able to exploit this methodology for the synthesis of natural products.[13]

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References

1 Kundig, E. P.; Cunningham Jr, A. F.; Paglia, P.; Simmons, D. P.; Bernadelli, G. *Helv. Chim. Acta*, **1990**, *73*, 386.

2 (a) Pike, R. D.; Sweigart, D. A. *SynLett*, **1990**, 565; (b) Chung, Y. K.; Sweigart, D. A.; Connelly, N. G.; Sheridan, J. B. *J. Am. Chem. Soc.*, **1985**, *107*, 2388; (c) Chung, Y. K.; Choi, H. S.; Sweigart, D. A.; Connelly, N. G. *J. Am. Chem. Soc.*, **1982**, *104*, 4245.

3 Astruc, D. *SynLett*, **1991**, 369.

4 Astley, D. K.; Astley, S. T. *J. Organomet. Chem.*, **1995**, *487*, 253.

5 (a) Angelici, R. J.; Blacik, L. J. *Inorg. Chem.*, **1972**, *11*, 1754; (b) Munro, G. A.; Pauson, P. L. *Isr. J. Chem.*, **1977**, *15*, 258; (c) Lee, S. S.; Jeong, E.; Chung, Y. K. *J. Organomet. Chem.*, **1994**, *483*, 115.

6 Chung, Y. K.; Willard, P. G.; Sweigart, D. A. *Organometallics* **1982**, *1*, 1053.

7 Gschwend, H. W.; Handon, A. *J. Org. Chem.*, **1975**, *40*, 2008.

8 Meyers, A. I.; Temple, D. L.; Haidukewych, D.; Mihelich, E. D. *J. Org. Chem.*, **1974**, *39*, 2787.

9 Doyle, M. P.; Wierenga, W.; Zaleta, M. A. *J. Org. Chem.*, **1972**, *37*, 1957.

10 Analytical Data: **6**, m.p.: 129.5 °C; IR υ/cm^{-1} (KBr): 1990 (s), 1930 (s), 1910 (s), 1640 (m), 1030 (m); ^1H NMR ($CDCl_3$) δ: 1.44 (6H, s, $2CH_3$); 3.56 (2H, m, H1 + H5), 4.09 (2H, m, CH_2); 4.78 (1H, m, H6), 4.96 (2H, m, H_2 + H_4); 5.74 (1H, m, H3), 7.06-7.58 (4H, m, Ar-H). **7**, m.p.: 174 °C; IR υ/cm^{-1} (KBr): 2051 (s), 2001 (s), 1760 (s), 1650 (s), 1602 (w), 1578 (w), 1517 (m), 845 (s); ^1H NMR ($CDCl_3$) δ: 1.70 (3H, s, CH_3); 1.92 (3H, s, CH_3); 3.47 (1H, m, H1/H4); 3.57 (1H, m, H1/H4); 4.01 (1H, d, J=10.2 Hz, H6); 4.69 (1H, d, J=10.2 Hz, H5); 4.84 (2H, AB, J=8.5, CH_2); 5.62 (2H, m, H2+H3); 7.57 (2H, m, Ar-H); 7.85 (2H, m, Ar-H). **9**, m.p.: 135 °C, IR υ/cm^{-1} (KBr): 3400 (s,br), 2037 (s), 1973 (s), 1735 (s), 1046 (m), 646 (m). ^1H NMR ($CDCl_3$) δ: 0.68 (3H, s, CH_3), 0.98 (3H, s, CH_3), 3.03 (1H, d, J=10.1 Hz, H6), 3.10 (1H, m, H1/H4), 3.28 (1H, m, H1/H4), 3.38 (2H, m, CH_2O), 3.61 (1H, d, J=15.8 Hz, H7), 3.93 (2H, 2 overlapping d, H5 +H7'), 5.31 (1H, m, H2/H3), 5.69 (1H, m, H2/H3), 7.08 - 7.20 (4H, m, Ar-H). All compounds gave safisfactory elemental analyses.

11 March, J. Advanced Organic Chemistry, 3rd Ed.,Wiley, New York, **1985**, P.814.

12 Williams, D. H.; Fleming, I. Spectroscopic methods in organic chemistry, 3rd Ed., McGraw-Hill, London, **1980**, P.106.

13 For related organoiron stategies for the synthesis of alkaloids see: (a) Astley, S. T.; Stephenson, G. R. *SynLett*, **1992**, 507; b) H. J. Knölker, *SynLett*, **1992**, 371.

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