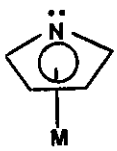
REACTIONS OF THE η^5-PYRROLYL LIGAND: A NEW CHALLENGE IN THE CHEMISTRY OF PYRROLES

Janusz Zakrzewski
Institute of Chemistry, University of Łódź
90-136 Łódź, Narutowicza 68, Poland

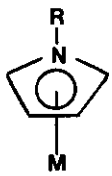
Abstract—This review describes reactions of the η^5-pyrrolyl ligand with special emphasis on their application in syntheses of substituted pyrroles.

INTRODUCTION

Reactions of hydrocarbon π-ligands (e.g. η^2-alkene, η^3-enyl, η^4-diene, etc.) in transition metal complexes have been extensively studied and have found widespread use in modern organic synthesis.[1] In contrast, surprisingly little is known about reactions of metal π-coordinated heterocycles.[2] Among five-membered systems only η^5-phospholyl and η^5-thiophene complexes have been studied in some detail, and recently reviewed[3,4] both showing original and rich reaction chemistry. The aim of this article is to bring into focus the chemistry of the transition metal coordinated pyrrole system. Pyrroles form several types of metal π-complexes, the most important being η^5-pyrrolyl (1) and η^5-pyrrole (2).



1



2

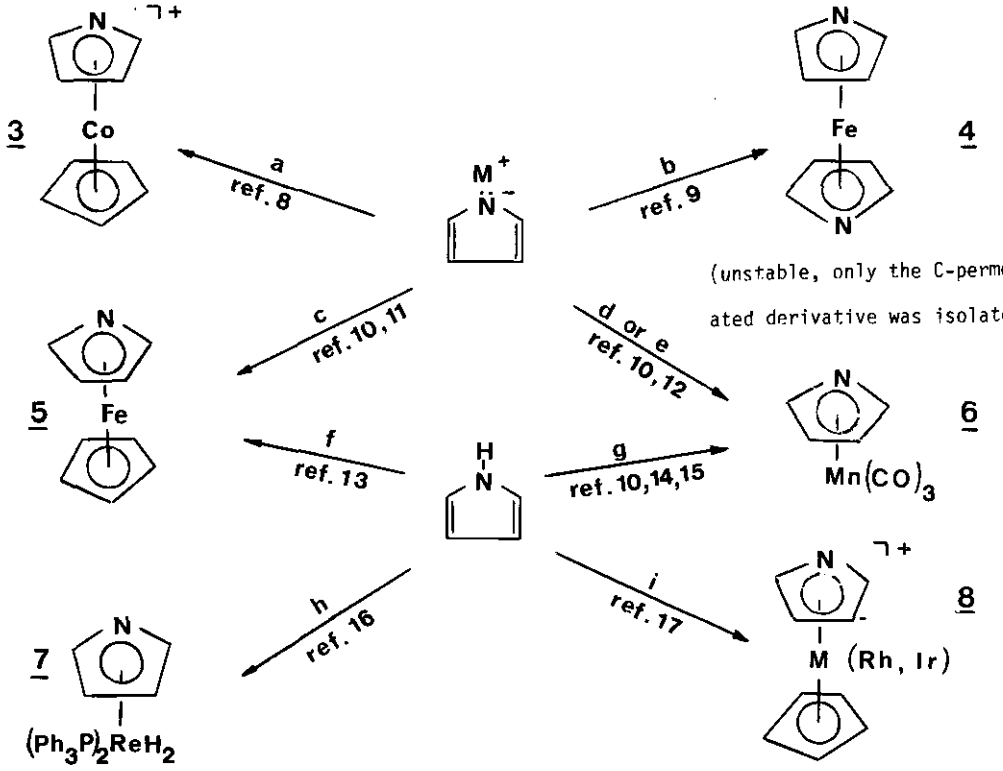
The complexes 1 and 2 are isoelectronic with the corresponding η^5-cyclopentadiene and η^6-arene carbocyclic systems, respectively. The known η^5-pyrrole complexes are kinetically rather unstable[5] and have so far not been explored. On the other hand, recent studies have shown that η^5-pyrrolyl complexes undergo a variety of highly selective reactions at the coordinated heterocycle. In my opinion, these reactions constitute a formidable challenge for the chemistry pyrroles e.g. enabling facile and selective introduction of substituents into this system. It should be mentioned that despite the tremendous research in this area the selective substitution

reactions of pyrroles remain relatively rare.[6] It is often easier to prepare a specifically substituted pyrrole (even a monosubstituted one) via ring synthesis (i.e. by cyclization of an appropriate acyclic precursor) rather than by a substitution reaction.

The η^5-pyrrolyl ligand displays an interesting, activating effect on the reactivity of the metal center. This area has been extensively explored and reviewed by Basolo et al.[7]

PREPARATION OF η^5-PYRROLYL METAL COMPLEXES

The synthetic routes leading to basic types of η^5-pyrrolyl transition metal complexes 3-8 are summarized in Scheme 1. Only ring unsubstituted compounds are shown for clarity.

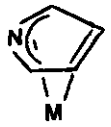


Syntheses of η^5-pyrrolyl transition metal complexes. Reagents:
(a) $(\eta^5\text{-}C_5H_5)Co(SMe_2)_3^{2+}$; (b) $FeCl_2$; (c) $(\eta^5\text{-}C_5H_5)Fe(CO)_2I$; (d) $Mn(CO)_5Br$;
(e) $Mn(CH_3CN)_3(CO)_3^{2+}$; (f) $(\eta^5\text{-}C_5H_5)Fe(CO)_2I$/diisopropylamine/$h\nu$; (g) $Mn_2(CO)_{10}$;
(h) $(Ph_3P)_2ReH_7$/3,3-dimethyl-1-butene; (i) $(\eta^5\text{-}C_5Me_5)M(OCOCF_3)_2(H_2O)$.

Scheme 1.

STRUCTURE AND STABILITY OF η^5-PYRROLYL METAL COMPLEXES

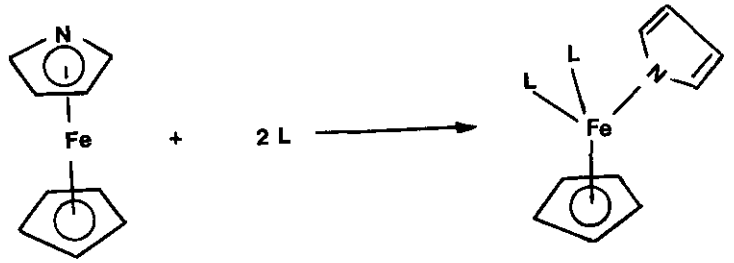
The bonding mode of the η^5-pyrrolyl ligand can be discussed in terms of wholly delocalized coordination 1 (analogous to that of the η^5-cyclopentadienyl ligand) or coordination involving η^3-azaallyl and η^2-olefinic subsystems 9.



9

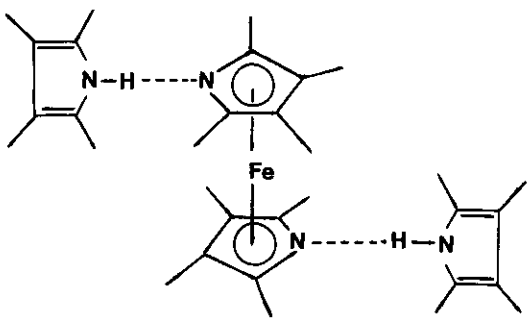
The latter structure has been postulated for the manganese complex 6 on the basis of ^{55}Mn NQR data.[18] More recently, a slippage of manganese from the pyrrolyl ring centroid toward nitrogen has been evidenced for the 3,4-dimethyl derivative of 6.[15] Such a slippage probably plays an important role in CO substitution reactions of 6.[7] Nevertheless, for the sake of simplicity the general representation of η^5-pyrrolyl complexes remains the structure 1.

η^5-Pyrrolyl complexes are as a rule less stable than their η^5-cyclopentadienyl counterparts. Whereas ferrocene is stable up to 470°C,[19] azaferrocene 5 decomposes already at 80°C[20] and 1,1'-diazaferrocene 4 (unknown) is considered highly unstable.[9] This intrinsic unstability is due to the high electronegativity of nitrogen which tends to act as a monodentate ligand only.[21] Such behavior can be illustrated by the reaction of azaferrocene 5 with π-acidic ligands L (CO, PF_3, isonitriles) in which $\eta^5 \rightarrow \eta^1$ transformation of the pyrrolyl ligand (but not the η^5-cyclopentadienyl ligand) is observed.[20]



5

Electron-withdrawing substituents in the pyrrole ring weaken its π-bonding ability and stabilize the η^1-coordinated species.[22] On the other hand, the introduction of alkyl substituents seems to stabilize η^5-pyrrolyl complexes. By virtue of such stabilization octamethyl-1,1'-diazaferrocene has recently been synthesized as a hydrogen-bonded adduct with two molecules of the parent pyrrole 10.[9]



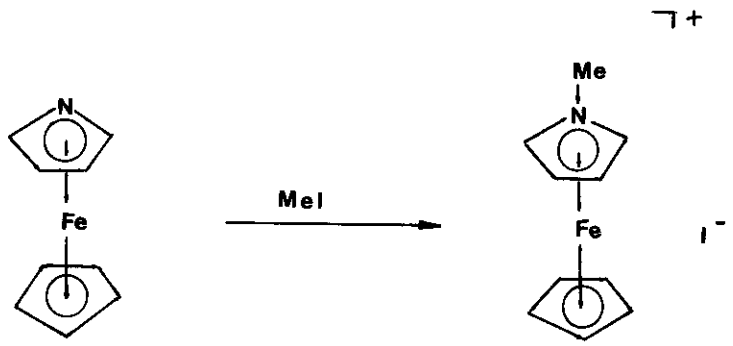
10

REACTIONS OF THE η^5-PYRROLYL LIGAND

Electrophilic attack at nitrogen

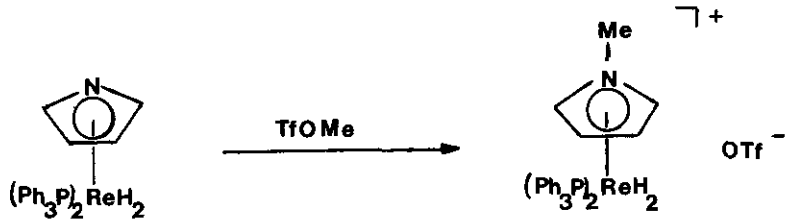
The lone pair of electrons on nitrogen endows the η^5-pyrrolyl ligand with basic and nucleophilic character. As expected, these properties depend largely on the nature of the metal center. For example, whereas azaferrocene 5 displays basic properties in aqueous solutions (pK_a = 4.5),[10] the manganese complexes 6 and (η^5-pyrrolyl)$Mn(CO)_2(PPh_3)$ are considerably less basic and undergo N-protonation only in CF_3COOH or CF_3COOH-CH_2Cl_2 media.[23,24]

Azaferrocene (5) reacts readily, at room temperature, with methyl iodide to afford rather unstable η^5-N-methylpyrrole complex 11.[10]



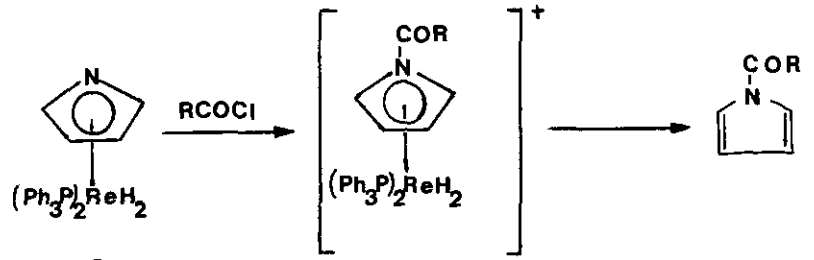
5 11

Less nucleophilic complexes 6 and 7 are not affected by methyl iodide. However, 7 is methylated at nitrogen by means of methyl triflate to give the cationic complex 12 in high yield.[16]



7 12

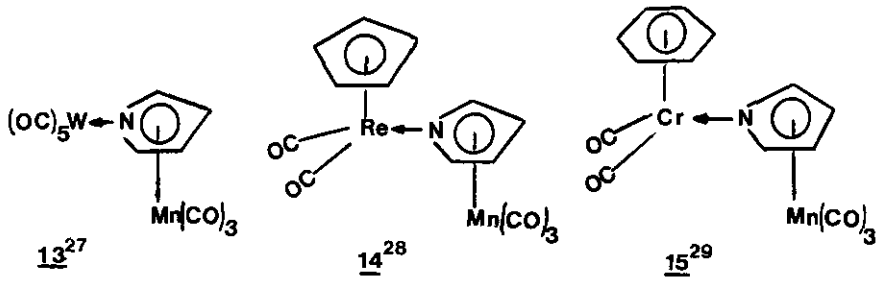
The reaction of 7 with acyl halides affords the corresponding N-acylpyrroles in high yield.[25] It can be rationalized by electrophilic attack at nitrogen, accompanied by spontaneous decomplexation of heterocycle accelerated by the electron-withdrawing effect of the acyl group. This reaction constitutes therefore a mild method of decomplexation of the pyrrole system.



7

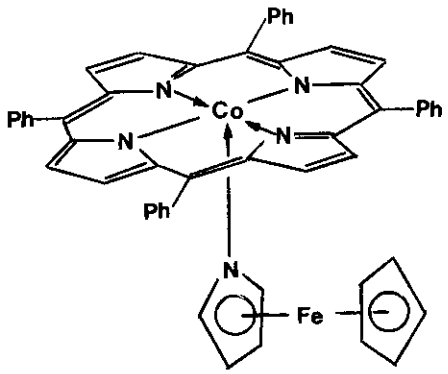
Similar, although uncomplete (30%) release of N-acylpyrrole was observed in the reaction of 6 with diphenylketene.[26]

The η^5-pyrrolyl ligand can act as a two electron donor nitrogen ligand toward electrophilic metal centers. In fact, chemistry of 6 is dominated by formation of bi- and trinuclear complexes containing η^1,η^5-bridging pyrrolyl ligand. Representative examples of such species are complexes 13-15.

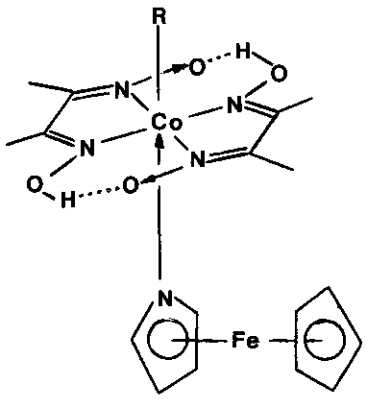


13[27] 14[28] 15[29]

N-Coordinating properties of azaferrocene are less known. Only very recently it has been demonstrated that it coordinates, similarly to pyridine, to the axial sites of cobalt (II) porphyrins and alkylcobaloximes to form heterobinuclear complexes 16-17.



16

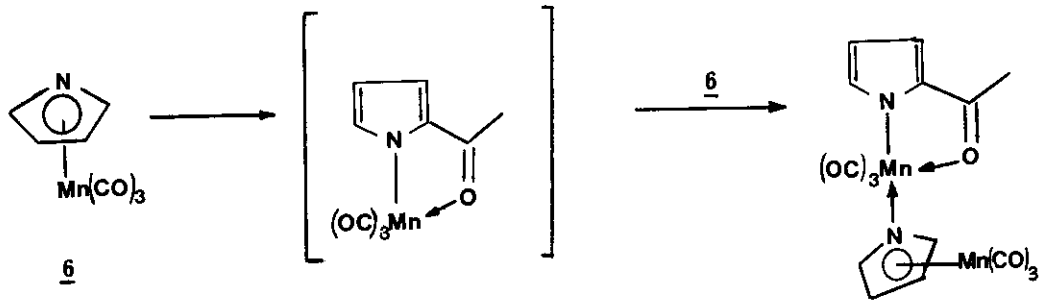


17

Electrophilic attack at carbon

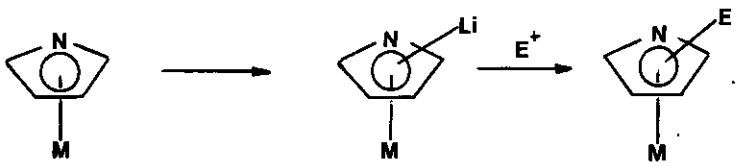
Electrophilic attack at carbon is less characteristic for the η^5-pyrrolyl ligand since its most nucleophilic site is situated at nitrogen. Moreover, the electrophilic addition to nitrogen can deactivate the η^5-pyrrolyl ligand towards subsequent electrophilic attack at carbon or results in decomposition of the complex. Nevertheless, a few examples of electrophilic C-substitution of the η^5-pyrrolyl ligand have been reported. The simplest one is the hydrogen-deuterium exchange in (η^5-pyrrolyl)$Mn(CO)_3$ in acid media.[30] Curiously, the rates of exchange in α- and β-positions are equal. Coordination of the pyrrole nitrogen in this complex to the $W(CO)_5$ moiety (complex 13) decreases the rate of exchange by a factor of about 40, conserving the lack of regioselectivity.[27]

The attempted acetylation of 6 by means of the acetic anhydride-phosphoric acid system gave the binuclear complex 19 containing the expected 2-acetylpyrrole ligand as a chelating species. However, half of the starting material remained unaffected, serving only as a η^1-N ligand stabilizing the intermediate 18.[31]

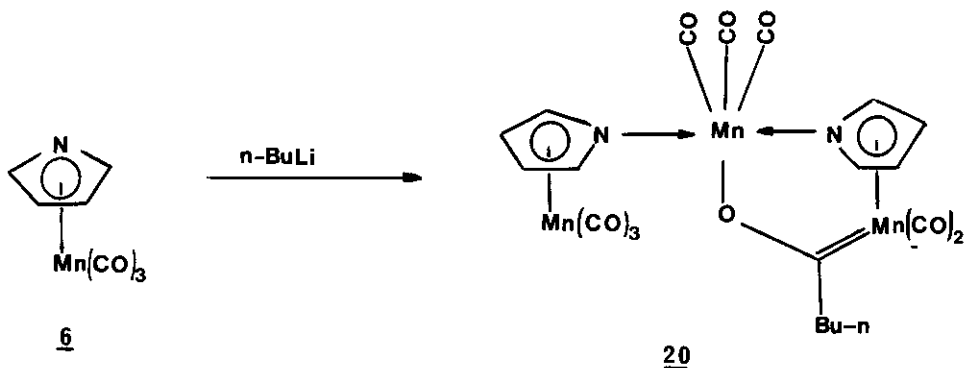


Up to now, all attempts to achieve electrophilic C-substitution of azaferrocene have been unsuccessful.

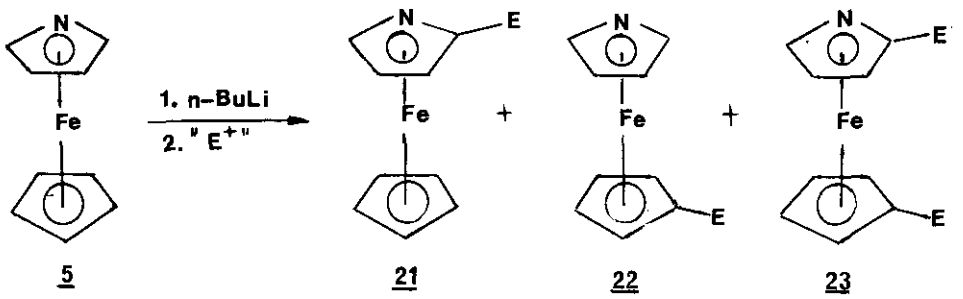
Obviously, it may be expected that metallation (lithiation) would result in enhancement of C-nucleophilicity enabling electrophilic C-substitution:



The evidence that such an approach is feasible has been supported only very recently. The complex 6 is not well suited for this scope since the metallating agent (n-BuLi) attacks the coordinated CO instead of the heterocyclic ligand, to afford the trinuclear complex 20.[32]

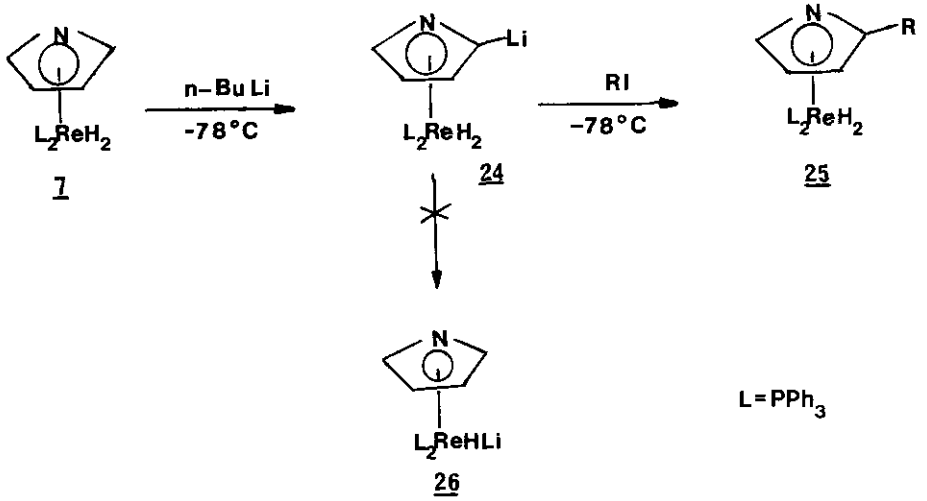


On the other hand, the η^5-pyrrolyl ligand in azaferrocene 5 can be readily metallated at the α-position by means of n-BuLi. Unfortunately in this case, however, the competitive lithiation of the η^5-Cp ligand takes place, leading, after quenching with an electrophile, to the complex reaction mixtures 21-23.[33]



"E^+" = Me^+(MeI) or $(Me)_3Si^+$ [$(Me)_3SiI$]

The exclusive lithiation of the η^5-pyrrolyl ligand in a transition metal complex was observed only very recently.[34] The treatment of the rhenium complex 7 with n-BuLi in THF at -78°C afforded the 2-lithio derivative 24, which reacted smoothly with alkyl iodides to give (η^5-2-alkylpyrrolyl) complexes 25 in high yield.

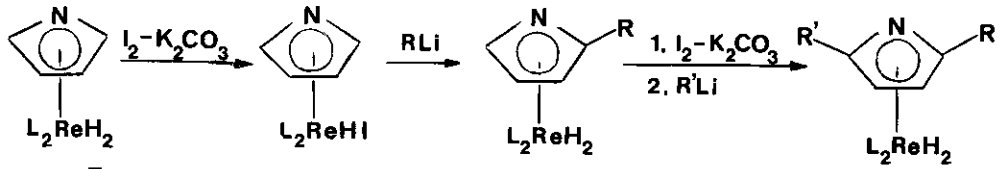


Fortunately, in this case the hydrogen migration 24 → 26 (very characteristic for the ring-deprotonated η^5-cyclopentadienyl metal hydrides)[35] does not occur at -78°C.

Nucleophilic attack at carbon

Pyrroles having no electron-withdrawing substituents (and obviously the corresponding pyrrolyl anions) are inert to nucleophilic addition or substitution reactions.[6] However, it may be expected that such reactions could be promoted by coordination of the pyrrole system to a strong electrophilic metal center (inversion of the charge affinity or "umpolung"). This expectation was confirmed in 1985.[16] The η^5-pyrrolylhydridoiodorhenium complex 27 (readily accessible from

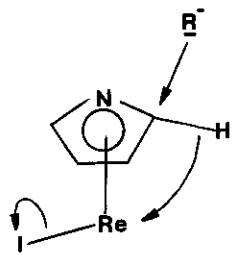
7 by treatment with I_2-K_2CO_3) reacts with alkyl- and aryllithiums to afford (η^5-2R-pyrrolyl)-rhenium dihydrides 28 in high yields and excellent (> 98%) regioselectivity.



7 27 25 28

L=PPh$_3$

This very unusual reaction consists of nucleophilic attack at C-2, migration of hydrogen from this carbon atom to rhenium and the elimination of a good nucleofuge (iodide). It proceeds either as an entirely concerted nucleophilic process (structure 29) or is initiated by electron transfer from RLi to 27.



29

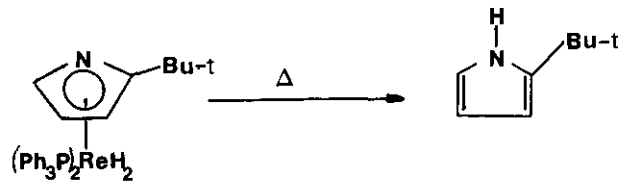
The most interesting feature of this transformation is that it can be easily repeated allowing the introduction of a second substituent into the η^5-pyrrolyl ligand (transformation 25 → 28). The isolation and purification at the hydridoiodo intermediate is not required and the reaction can be performed under "one flask" conditions.

Unfortunately, attempts to repeat this procedure a third time and introduce a third substituent to the η^5-pyrrolyl ligand failed. Although the iodination takes place normally, the reaction with RLi is very slow and gives complex untractable mixtures.

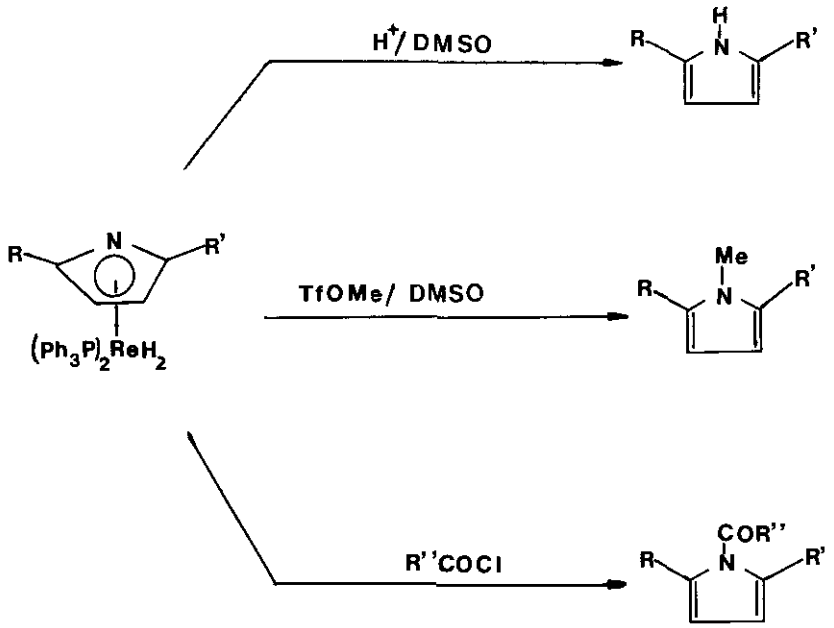
The presented approach opens some novel opportunities for synthesis of substituted η^5-pyrrolyl rhenium complexes and corresponding pyrroles. For example, it enables the easy introduction to the pyrrole system of one or two aryl or/and alkenyl substituents, that up to now have constituted a difficult synthetic problem. However, it should be noted that complex 27 is reactive only towards highly nucleophilic alkyl- or aryllithium reagent and fail to react with less nucleophilic species e.g. enolates.

Decomplexation methods

The only η^5-pyrrolyl complexes studied for the purposes of developping of mild and efficient methods of decomplexation of the co-ordinated heterocycle are rhenium complexes 7, 25 and 28.[25] These complexes are surprisingly stable (up to 150°C). Their pyrrolysis at higher temperatures leads to the liberation of triphenylphosphine rather than pyrrole. Only in the case of complexes having bulky t-butyl substituents formation of the corresponding pyrrole was observed[16] e.g.:



A more general decomplexation method consists of the reaction of these complexes with an electrophile, followed by treatment with DMSO, which remplaces the kinetically labile η^5-pyrrole ligands (Scheme 2).[25] In the case of RCOCl decomplexation of N-acylpyrrole proceeds spontaneously.

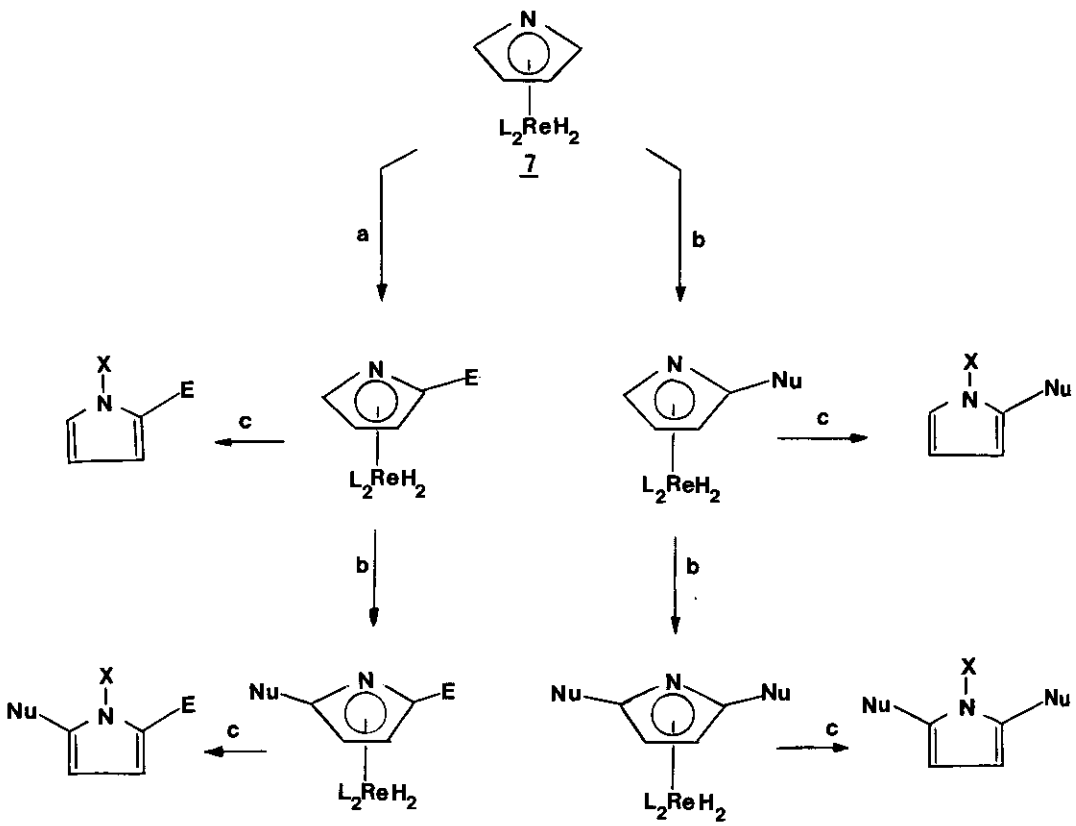


Decomplexation of pyrroles from (η^5-pyrrolyl)bis(triphenylphosphine)rhenium dihydrides.

Scheme 2.

Concluding remarks

The results presented here (especially those obtained for rhenium complexes) clearly indicate that η^5-pyrrolyl transition metal comlexes are versatile intermediates in synthesis of substituted pyrroles via substitution reactions. Either classical electrophilic as nucleophilic C-substitution is possible (Scheme 3).



Synthesis of substituted pyrroles from 7. L = PPh_3; E = alkyl; Nu = alkyl, alkenyl, aryl; X = H, alkyl, acyl.

Reagents: (a) 1. n-BuLi/RI; (b) 1.I_2-K_2CO_3 2. RLi; (c) HBF_4/DMSO or TfOMe/DMSO or RCOCl.

Scheme 3.

Although determination of the scope and limitations of these reactions is in need of further studies, their synthetic potential is already considerable. All processes involved in Scheme 3

occur in high, virtually quantitative yields and with excellent regioselectivity. All rhenium complexes shown are crystalline yellow or orange air stable compounds, which under mild conditions easily loose the corresponding NH or N-substituted pyrroles. To complete, the starting complex 7 is easily accessible from commercially available perrhenic acid:

$$HReO_4 \xrightarrow[CH_3COOH\text{-}HCl]{PPh_3} (Ph_3P)_2ReOCl_3 \xrightarrow{LiAlH_4} (Ph_3P)_2ReH_7{}^{36} \xrightarrow{pyrrole/t\text{-}BuCH=CH_2} 7^{16}$$

However, the relatively high cost of this reagent should be noted (7-8 US $/g at Aldrich), which constitutes a serious limitation of the application of this approach to large-scale preparations of pyrroles. It can be therefore expected that future trends in this field will concentrate on the use of cheaper transition metals (e.g. iron). Among numerous problems that may be resolved in the near future by using η^5-pyrrolyl metal comlexes one can mention the activation of the lateral alkyl chain in pyrroles towards the proton loss and the use of homochiral pyrrolyl complexes in enantioselective syntheses of pyrroles and pyrrolidines.

ACKNOWLEDGMENT

The financial support from the Polish Academy of Sciences (Research Project CPBP 01.13) is gratefully acknowledged.

REFERENCES

1. J. P. Collman and L.S. Hegedus, 'Principles and Application of Organotransition Metal Chemistry,' *University Science Books*, Mill Valley, 1980; S.G. Davies, 'Organotransition Metal Chemistry: Application to Organic Synthesis,' Pergamon Press, Oxford, 1982.
2. For general aspects of transition metal π-complexes of heterocycles see: K.H. Pannell, B.L. Kalsotra, and C. Párkanyi, J. Heterocycl. Chem., 1978, 15, 1057. G.M. Bogdanov and Yu. G. Bundel, Khim. Geterosikl. Soed., 1983, 8, 1155.
3. F. Mathey, New J. Chem., 1987, 11, 585.
4. R. J. Angelici, Acc. Chem. Res., 1988, 21, 387.
5. K. Ofele and E. Dotzauer, J. Organometal. Chem., 1971, 30, 211.

6. R. J. Sundberg, 'Comprehensive Heterocyclic Chemistry,' Vol. 4, ed. by A. R. Katritzky and C. W. Rees, Pergamon Press, Oxford, 1984, pp. 313-377.
7. D. L. Kershner and F. Basolo, Coord. Chem. Rev., 1987, 79, 279.
8. N. Kuhn, G. Brüggemann, M. Winter, and V. M. De Bellis, J. Organometal. Chem., 1987, 320, 391.
9. N. Kuhn, E.-M. Horn, R. Boese, and N. Augart, Angew. Chem. Int. Ed. Engl., 1988, 27, 1368. Compare: W. K. Reagen and L. J. Radonowich, J. Am. Chem. Soc., 1987, 109, 2193.
10. K. K. Koshi, P. L. Pauson, A. R. Quazi, and W. H. Stubbs, J. Organometal. Chem., 1964, 1, 471.
11. K. Bauer, H. Folk and K. Schlögl, Angew. Chem. Int. Ed. Engl., 1969, 2, 135.
12. L.-N. Ji, D. L. Kershner, M. R. Rerek, and F. Basolo, J. Organometal. Chem., 1985, 297, 83.
13. J. Zakrzewski, J. Organometal. Chem., 1987, 327, C41.
14. D. L. Kershner and F. Basolo, J. Am. Chem. Soc., 1987, 109, 7396.
15. D. L. Kershner, A. L. Rheingold, and F. Basolo, Organometallics, 1987, 6, 196.
16. H. Felkin and J. Zakrzewski, J. Am. Chem. Soc., 1985, 107, 3374; J. Zakrzewski, J. Organometal. Chem., 1987, 333, 71.
17. C. White and P. Maitlis, J. Chem. Soc. (A), 1971, 3322.
18. M. D. Fayer and C. B. Harris, Inorg. Chem., 1969, 8, 2792.
19. A. J. Deeming, 'Comprehensive Organometallic Chemistry', Vol. 4, ed. by Sir G. Wilkinson, Pergamon Press, Oxford, 1982, p. 478.
20. A. Efraty, N. Jubran, and A. Goldman, Inorg. Chem., 1982, 21, 868.
21. F. Seel and V. Sperber, J. Organometal. Chem., 1968, 14, 405.
22. P. L. Pauson, A. R. Quazi, and B. W. Rockett, J. Organometal. Chem., 1967, 7, 325.
23. D. N. Kursanov, V. N. Setkina, and N. I. Pyshnograeva, Izv. Akad. Nauk SSSR, Ser. Khim., 1984, 878.
24. N. I. Pyshnograeva, A. S. Batsanov, Yu. T. Struchkov, and A. G. Ginsburg, J. Organometal. Chem., 1985, 297, 69.
25. J. Zakrzewski, J. Organometal. Chem., 1987, 326, C17.
26. W. A. Herrmann, I. Schweizer, P. S. Skell, M. Ziegler, K. Weidenhammer, and B. Nuber, Chem. Ber., 1979, 112, 2423.
27. N. I. Pyshnograeva, V. N. Setkina, and D.N. Kursanov, Izv. Akad. Nauk SSSR, Ser. Khim., 1981, 654.
28. N. I. Pyshnograeva, V. N. Setkina, V. G. Andrianov, Yu. T. Struchkov, and D. N. Kursanov, J. Organometal. Chem., 1978, 157, 431.
29. V. I. Losilkina, N. I. Pyshnograeva, N. K. Baranetskaya, and V. N. Setkina, Izv. Akad. Nauk SSSR, Ser. Khim., 1985, 2780.

30. N. V. Kislyakova, N. I. Pyshnograeva, V. F. Sizoy, N. E. Kolobova, V. N. Setkina, and D. N. Kursanov, Dokl. Akad. Nauk SSSR, 1973, 212, 367.

31. N. I. Pyshnograeva, V. N. Setkina, V. G. Andrianov, Yu. T. Struchkov, and D. N. Kursanov, J. Organometal. Chem., 1977, 128, 381.

32. N. I. Pyshnograeva, V. N. Setkina, V. G. Andrianov, Yu. T. Struchkov, and D.N. Kursanov, J. Organometal. Chem., 1981, 206, 169.

33. N. I. Pyshnograeva, V. N. Setkina, and D. N. Kursanov, J. Organometal. Chem., 1983, 251, C41.

34. J. Zakrzewski, J. Organometal. Chem., 1989, 362, C31.

35. M. C. Milletti and R. Fenske, Organometallics, 1989, 8, 420 and references therein.

36. D. Baudry, M. Ephritikhine, and H. Felkin, J. Organometal. Chem., 1982, 224, 363.

Received, 30th October, 1989