Group 9 open-shell organometallics: reactivity at the ligand
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Chapter 8

Perspective:

Ligand Radicals in New, Catalytic Reactions
8.1 Introduction

Unlike the uncontrolled reactivity of free organic radicals in solution, the reactivity of transition metal coordinated ‘ligand radicals’ can proceed in a highly selective manner. Several bio-enzymatic processes take effective advantage of the controllable reactivity of ligand radicals, thus allowing highly chemo-, regio-, diastereo- and enantio-selective radical-type reactions to achieve transformations that are not easy to achieve via closed-shell reaction pathways. These enzymatic radical-type reactions frequently exploit the features of so-called ‘redox non-innocent’ ligands; ligands that are easier to oxidize or reduce than the transition metal to which they coordinate. The combined, cooperative action of the radical-type reactivity of the redox non-innocent ligand and the substrate coordinating and activating properties of the transition metal, allows the enzyme to catalyze ‘difficult reactions’ with unprecedented rates and selectivities. This concept has inspired many synthetic chemists to employ similar principles in the field of organometallic chemistry, the playground of catalytic synthetic-organic transformations. Several stoichiometric open-shell organometallic reactions involve prior formation of ‘ligand radicals’, followed by ligand-centered transformations. Many of such ligand-centered radical-type reactions proceed in a controlled and selective manner, most frequently leading to metal-carbon and carbon-carbon radical-couplings. For the more sterically hindered systems selective ligand-centered hydrogen atom abstractions are a common alternative reaction pathway. These selective ligand-centered radical-type reactions are synthetically useful in organometallic synthesis, allowing interesting ligand transformations and the formation of tethered binuclear organometallic compounds, for example. Some of the observed stoichiometric transformations serve to explain unwanted side-reactions and catalyst deactivation pathways in existing (open-shell and closed-shell) catalytic reactions. Other unusual and selective radical-type ligand-ligand C−C and C−O coupling reactions are inspiring from an organic-synthetic point-of-view, and may eventually lead to applicable new catalytic transformations. In this Thesis, we have shown that synthetic catalytic reactions actually can operate via selective organometallic radical-coupling processes, thus allowing highly chemo-, regio-, diastereo- and even enantioselective turnover (see Chapter 4). New insights in the catalytic mechanism of these Co(por) mediated olefin cyclopropanation reactions revealed that the ‘redox non-innocence’ of the terminal carbene ligand plays a crucial role, and the cooperative action of the ‘carbene radical’ and the transition metal is an essential feature in the substrate activation and conversion process. These new insights clearly show that bio-inspired, enzyme-like approach can be employed in synthetic organometallic catalysis to achieve selectivity in radical-type transformations. If this is possible for radical-type olefin cyclopropanation reactions, why should it not be possible for other radical-type transformations?

Let us set our imagination free and think about the possible new reactions that could be developed on the basis of the redox non-innocence of the carbene ligand.

8.2 Broadening the scope of reactivity of carbene radicals

It is now well established that the carbene radicals allow for easy cyclopropanation of otherwise difficult (electron-poor) substrates. One of the possible ways to expand the scope of their reactivity could be the utilization of carbene precursors
with a conjugated double bond (Figure 1A). A properly designed precursor (i.e. leading to radicals being highly stabilized at the carbon containing the R2 group) should allow for additions of the γ carbon radical to olefinic substrates. Addition to an olefin would lead to an ε radical and subsequent ring closure could yield a cyclopentene derivative.

Another route toward highly substituted cyclopentenes could be possible with functionalized conjugated dienes (Figure 1B). This reaction would proceed via intermediates similar to the ones in pathway A and again, proper design of the reacting diene should play a key role in allowing such reactivity.

![Figure 1](image1.png)

**Figure 1.** Theoretical radical mechanisms involving redox non-innocence of carbenes leading to highly functionalized cyclopentenes.

The calculated spin density plot of a possible intermediate from pathway A is presented in Figure 2. DFT calculations suggest that in analogy to the one-electron reduced vinylcarbenes of Cr and W, the radical-type reactivity should be possible on the γ carbon.

![Figure 2](image2.png)

**Figure 2.** Calculated (Turbomole, RI-DFT, BP86, SV(P)) spin density plot of the Co(por)(OC(O)Me)(CHCHPh) complex showing substantial delocalization of the unpaired electron over the α and γ carbon atoms. The numbers represent the calculated spin densities on the respective atoms.
Another field in which the carbene radical complexes could be used is perhaps organometallic controlled radical co-polymerization of olefins with diazo compounds (Figure 3).\(^{3,4}\)

**Figure 3.** Possible incorporation of carbene radicals into the growing polyolefin chain.

In such a hypothetical reaction, the radical carbene complex could occasionally react with the growing polymeryl radical chain built from C2 units. This would allow the incorporation of C1 units into the polyolefinic polymer. Subsequent homolytic cleavage of the M–C bond would regenerate the active polymeryl radical chain (elongated by one carbon atom of the diazo compound) and allow its further radical polymerization, just like in the standard OMRP. The metal radical could react further with either a diazo compound to form a new radical carbene, or with the growing polymer chain to form a dormant species. Combining C2 with C1 radical polymerization could lead to functionalized polymers with interesting structures and properties.

To attain high incorporation of the C1 units into the polymer chain, very reactive diazo compounds should be utilized since the barriers for formation of radical carbenes from diazoacetates are rather high\(^{1a,b}\) and the amount of the free metal radicals during the metal mediated radical polymerization is very low.\(^5\) Thus, diazoalkanes should be good candidates as the radical carbene sources in combination with olefinic monomers which allow for easy cleavage of M–C bonds (i.e. their radicals should have high radical stabilization energy) like methyl methacrylate.

### 8.3 Redox non-innocence in other catalytic reactions?

Nitrenes are nitrogen analogues of carbenes (Figure 3) and could also be redox non-innocent. Metal nitrenes are involved in aziridination of olefins or C-H insertion reactions.\(^6\) Possible radical pathways were postulated,\(^7,8\) but up to now no spectroscopic evidence for the existence of nitrene radical ligands has been presented.

**Figure 4.** Hypothetical redox non-innocent behavior of nitrenes.
Our preliminary DFT calculations suggest that the putative tosylnitrene intermediate in cobalt(II) porphyrin catalyzed aziridinations indeed has a substantial spin density located on the nitrogen ligand, showing a strong analogy with carbene radicals (Figure 4). Therefore it seems that detection of nitrene radicals experimentally with EPR spectroscopy could be feasible and would provide a definite proof for the redox-non innocence of the nitrene group. As a result, reactions analogous to the ring-closure reactions shown in Figure 1 could be possible with nitrene precursors, which would provide a convenient new synthetic route to prepare functionalized dihydro-pyrroles.

![Figure 5](image_url)

**Figure 5.** Calculated (Turbomole, RI-DFT, BP86, SV(P)) spin density plot of the Co(por)NSO₂Ph complex showing substantial localization of the the unpaired electron on the nitrogen p orbital. Calculated spin densities: Co: 27.9%; N: 62.8%; S: –0.2%; O: 7.9 and 6.5%.

### 8.3 Conclusions

Throughout the Thesis we have shown that the concept of ligand redox-non innocence can be utilized not only in stoichiometric, but also catalytic reactions. One electron activation of the coordinated ligand leads to a dramatic change in the reactivity pathways allowing for reactions with otherwise not reactive substrates. The reactivity of radical carbenes described in Chapters 1, 5 and 6 is an archetypical example of this phenomenon. In this Perspective we propose that one can take advantage of the unusual electronic structure of the carbene radical in catalytic reactions other than cyclopropanation. Formation of five membered rings incorporating a carbene or nitrene moiety in reaction with (di)olefin or radical co-polymerization of carbenes with olefins are examples of such possible transformations.

Hence, we firmly believe that open-shell organometallic chemistry in general has a bright (catalytic) future. Much can be expected from future computational studies and conscientious spectroscopic investigations of open-shell organometallic compounds, which should provide valuable and detailed new information about their intriguing and unusual electronic structures. This will be of crucial importance for further synthetic developments, especially in the realm of catalysis.
Notes and References


4  C1 polymerization of carbenes has been recently reviewed: Jellema, E.; Jongerius, A. L.; Reek J. N. H.; de Bruin B. Chem. Soc. Rev. 2010, 39, 1706-1723.

5  For example, the dissociation equilibrium constant at 333K for organo-cobalt complexes formed in Co(por) mediated radical polymerization of methyl acrylate was estimated as 1.15·10-10: Peng, C.-H.; Li, S.; Wayland, B. B. Inorg. Chem. 2009, 48, 5039-5046.


10 This analogy can be also found in the oxo ligand of cytochrome P450 which is redox non-innocent and undergoes C–H bond insertion proceeding via a two step radical process.