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Cycloruthenated Compounds – Synthesis and Applications

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The syntheses of cycloruthenated compounds by several methods, and especially by the C–H activation pathway, have been reviewed. Many ruthenium-containing starting materials lead to these interesting organometallic compounds, which have found various applications in different fields of chemistry. Their reactivity highlights both the variety of reactions that were found to occur at the Ru–C bonds as well as the inertness of the organometallic moiety when these species are exposed to strongly oxidizing molecules or to reactive halogenation reagents. Their use as catalyst precursors showed them to be particularly efficient for hydrogenation reactions, either by H_2 or by hydride transfer. Physicochemical characteristics of cycloruthenated complexes include: (i) a cathodic shift of the electrochemical potentials corresponding to various redox couples, (ii) a bathochromic shift of UV/Vis absorption bands, (iii) valuable luminescence properties. Dinuclear cycloruthenated complexes display specific properties connected to interactions between the metals, such as strong electronic coupling, evidenced by intervalence bands of mixed-valence species, or efficient energy transfer.

1. Introduction

The cyclometallation of ligands by transition metals is one of the oldest reactions leading to organometallic compounds, known since the early 1960s, and hence one of the best developed areas of organometallic chemistry.[1] It was soon recognized to be the easiest way of formation of a transition-metal complex with a carbon–metal bond; moreover, as these compounds proved generally to be rather stable, they were also easy to characterize. Thus, thousands of papers dealing with these compounds have been published during the last 40 years.[2] The most popular way to achieve the synthesis of cyclometallated complexes was the route involving C–H activation procedures, and therefore this reaction was and still is considered an important model for the C–H activation of hydrocarbons by transition metals. Several applications of this class of compounds, such as the use of cyclometallated compounds as chiral auxiliaries, as mesogenic and photoluminescent compounds, as well as their potential use in biology, contributed significantly to the popularity of this research theme.[3] Since the discovery of the cyclometallation reaction, many transition metals have been successfully used to lead to this type of organometallic compounds. Palladium is without any doubt the transition metal that has been the most studied, as cyclopalladated compounds are known for nearly all classes of ligands to date. Renewal of interest in these compounds emerged ten years ago when some of them were identified as powerful catalysts for the formation of C–C or C–Y (Y = heteroatom) bonds,[4–9] since unprecedented TON or TOF numbers were obtained for reactions involving cyclopalladated compounds as catalyst precursors. It is obvious that the corresponding ruthenium derivatives, i.e. the cycloruthenated compounds, have been much less studied than the cyclopalladated ones. It is well known that ruthenium derivatives could have behaviours complementary to those of their palladium counterparts. It is therefore the aim of this review article to show the high potential that these organoruthenium compounds may have. After summing up various aspects of the synthesis of cycloruthenated compounds, we highlight the different applications in various fields of chemistry that these compounds are leading to.

2. Cycloruthenation

For anyone dealing with the chemistry of ruthenium complexes, cycloruthenation appears to be a rather opaque process. Cycloruthenation has incited astonishment and stimulated the interest of numerous researchers since the early 1970s. Whilst preparing this review, it appeared rather difficult to draw a structured presentation along the lines of what could be the specific mechanistic features of the cycloruthenation of aromatic ligands. For a given family of

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metallating agents, we found more disagreeing opinions or unsupported statements than actual facts that could clarify the nature of mechanisms. In other words, the lack of sound mechanistic information prevented us from making a systematic classification of cycloruthenations based on classes or types of mechanisms, i.e., S_EAr-like with arenium-like intermediates or "concerted" with multicentre agostic-type intermediates. A "minimalistic" option, i.e., a classification based on the nature of the metallating agent, was rather preferred. Nonetheless, it can be foreseen that with the present pace of development of computational methods and the revived interest for cyclometallation among theoreticians,[10–12] sufficient base for further rationalization of the reactivity of ruthenium complexes will be soon conveyed to experimentalists.

At this point we identified three main classes of cycloruthenation reactions (Figures 1 and 2), namely: (1) ruthenation by C–H bond activation, (2) transmetallation or ligand-exchange reaction and (3) all remaining isolated cases of activation of a carbon–element bond, wherein the element is neither hydrogen nor a metal.

In the following, the reader will find a nonexhaustive inventory of these types of cycloruthenation reactions subdivided by types of metallating agents that have appeared in the literature between 1970 and 2007 (Figure 1). Fortuitous and intentional syntheses of cycloruthenated complexes are reviewed herein, because both of them provide elements of information on the peculiarity of the chemistry of ruthenium complexes. As depicted in Figure 1, several types of ruthenium complexes have been investigated. Some, found to be already efficient in the C–H bond activation route, found their way in C–M and C–Y activation routes. The literature establishes the versatility of $RuCl_2(\mathbf{P})_3$ complexes, a class of coordination complexes for which applications in all three routes have been reported. Many reports deal with cycloruthenation involving the so-called C–H bond activation route. All oxidation states are considered for the Ru centre, although Ru^{II} complexes are the most frequent. The precedence of carbonylruthenium complexes of various formal oxidation states and nuclearities must also be outlined. The transmetallation reaction, intentionally termed here as the "C–M activation" route, has been covered with a nar-

Jean-Pierre Djukic, born in 1967, obtained his Ph. D. in 1992 under the supervision of Dr. Eric Rose at the University Pierre et Marie Curie (Paris, France). After a postdoctoral stay at Iowa State University in Ames (IA, USA) with Prof. L. Keith Woo, he obtained a permanent appointment at the CNRS in 1994. In 1996 the Alexander von Humboldt Foundation granted him a fellowship to collaborate with Prof. Dr. Karl Heinz Dötz at the Rheinische Friedrich Wilhelms Universität in Bonn. Since 1994 he joined the team led by Dr. Michel Pfeffer in Strasbourg, where he is currently heading a research effort in organometallic chemistry. His themes of research encompass a large spectrum of applications of cyclometallated complexes, with particular emphasis on the development of new methodologies towards chiral metallacycles and on the synthesis of new functional compounds for molecular electronics.

Michel Pfeffer was educated at the Université Louis Pasteur in Strasbourg, and he has been Directeur de Recherche (CNRS) at this university since 1985. He has long been working on organic synthesis mediated and catalyzed by transition metals such as palladium and ruthenium derivatives. In this respect, he has mostly been interested in C–H activation processes and he was involved, since the early 1980s, in several functionalizations of C–H bonds through C–C and C–heteroatom bond syntheses occurring by cyclopalladation and cycloruthenation reactions. His current research interests are in coordination and organometallic chemistry of platinum group metals with an emphasis on the applications of organometallic compounds in various domains such as homogeneous catalysis and/or biology.

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Jean-Baptiste Sortais graduated from the École Normale Supérieure de Lyon (France) and received his M. Sc. in organic chemistry from the Université Louis Pasteur, Strasbourg, where he completed his Ph. D. in 2007 under the supervision of Dr. M. Pfeffer. After a postdoctoral stay with Prof. J. E. Bäckvall at Stockholm University, he is currently a postdoctoral fellow in the group of Prof. G. Erker at the University of Münster (Germany), working on the metal-free activation of hydrogen.

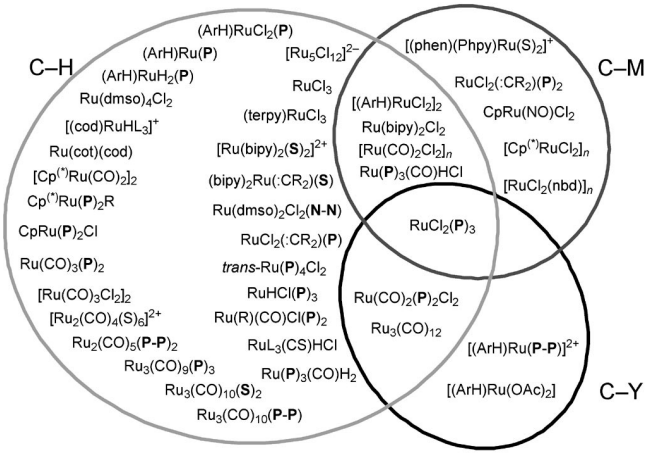


Figure 1. Classes of ruthenium complexes capable of sustaining cyclometallation of external or Ru-bound ligands by C–H (carbon–hydrogen), C–M (carbon–metal) and/or C–Y (carbon–element) activation. (**P**: any trivalent phosphorus ligand; **P-P**: any bis(phosphorus)-based ligand; **N-N**: a nitrogen-based ligand; **S**: solvent; ArH: benzene or *p*-cymene).

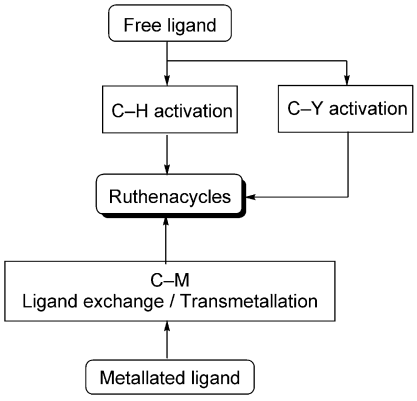


Figure 2. Synoptic diagram of the main synthetic routes toward cycloruthenated aromatic ligands.

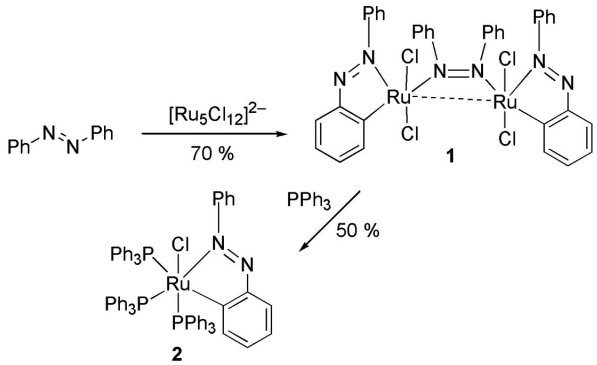
rower range of ruthenium complexes: it remains, however, the more reasonable substitute to unsuccessful cyclometallation by the C–H bond activation route.

2.1. The "C–H Bond Activation" Route: a Complexwise Inventory

The common denominator of cycloruthenation reactions that proceed through cleavage of a C–H bond at a potentially bidentate aromatic ligand is the formation of ruthenacycles, mostly five-membered and in some cases six-membered. Notwithstanding the intrinsic nature of the mechanism of such processes, which in most cases is still a matter of investigation, steric and electronic factors influence the fate of the cyclometallation in many ways. The presence of a formal external or internal base is often required but not mandatory. Last but not least, a no-brainer in some way, the existence of free coordination sites at the Ru centre, whatever its formal oxidation state, is a condition for the feasibility of the cyclometallation itself. In this section, we distinguish between ruthenium complexes on the basis of the local coordination geometry existing at the ruthenium centre and on the basis of their nuclearity. Carbonylruthenium complexes are addressed separately from other complexes, as they show a specific reactivity. There is no distinction based on the formal oxidation state at the Ru centre of the metallating agent, as we noticed that cyclometallations occurring by C–H bond cleavage were not necessarily isohypsic from the point of view of the metal centre. For example, Ru^0 as well as Ru^{III} reagents may well be used to produce Ru^{II} metallacycles.

Inorganic Ruthenium Complexes

$[Ru_5Cl_{12}]^{2-}$, a soluble subrogate of the fictitious $[RuCl_2]$, also known as "blue ruthenium chloride", was shown in the early 1970s by Wilkinson et al. to react with azobenzene to form in 70% yield a bisruthenacyclic complex, **1**, wherein both ruthenium centres reportedly bore the +3 oxidation state (Scheme 1).[13] The latter could readily be converted to its Ru^{II} parent, **2**, upon reaction with PPh_3, which putatively acted as a reducing agent.

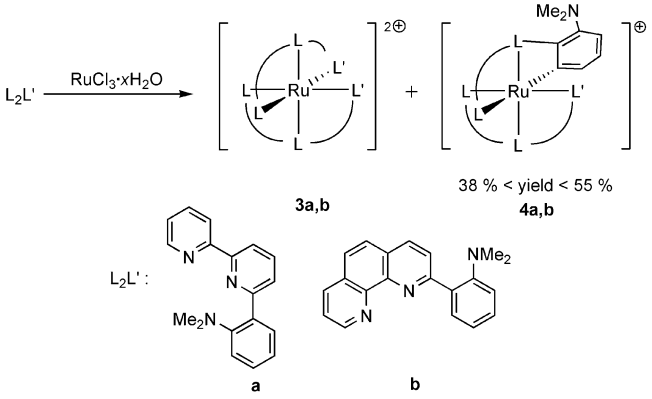


Scheme 1. Cycloruthenation of azobenzene by using "blue ruthenium chloride".

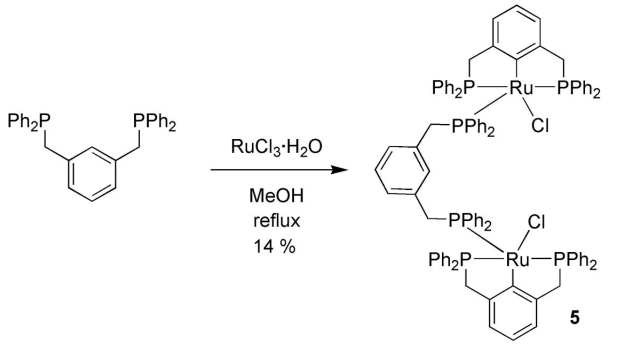
$RuCl_3$ hydrate was also reported to enable cyclometallation reactions, essentially with cluttered tridentate ligands derived from 2,2-bipyridine and phenanthroline.[14] Moderate yields in Ru^{II} metallacycles **4a**,**b** could be obtained upon treatment of the ligands with $RuCl_3$ hydrate in refluxing glycol (Scheme 2), the C–H bond cleavage process obviously competing with the conventional reductive coordination of the tridentate ligand to yield **3a**,**b**.

Tridentate ligands of the pincer PCP type have also displayed some reactivity towards $RuCl_3 \cdot 3H_2O$.[15] A typical reaction carried out in boiling methanol would only yield low amounts of a dinuclear bridged species **5** (Scheme 3).

Ruthenium solvates such as $[Ru(dmso)_4Cl_2]$ (Ru^{II}) or $[Ru(dmso)_2Cl_4][H(dmso)_2]$ (Ru^{III}) were found to produce fair yields of ruthenacyclic compounds of various ligands such as 6-aryl, 2,2′-bipyridines[16] and guanine derivatives.[17]



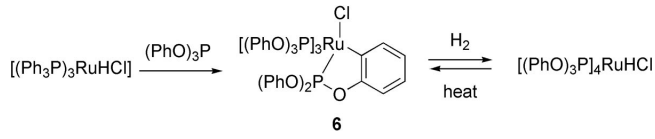
Scheme 2. Direct cycloruthenation of heterotridentate ligands by ruthenium trichloride hydrate.



Scheme 3. Direct cycloruthenation of a pincer ligand with ruthenium trichloride.

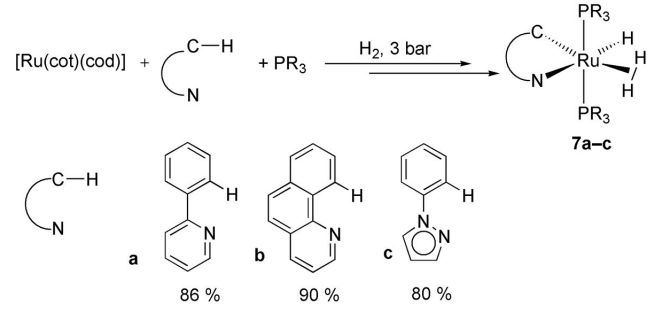
Ruthenium Coordination Complexes

In the years 1968 and 1969, the first cases of cycloruthenation reaction with $[(Ph_3P)_3RuHCl]$ were disclosed in independent reports by Levison and Robinson[18,19] and by Parshall, Knoth and Schunn.[20] The latter authors stressed that one outstanding feature of the reaction involving triaryl phosphites is its reversibility (Scheme 4). Treatment of ruthenacycle **6** with H_2 would yield a new hydridoruthenium compound (Scheme 4). This reversibility was exploited by Parshall[20] and elegantly improved by Lewis, who devised a catalytic system allowing the effective *ortho*-deuteration of phenol upon treatment with D_2 in the presence of the cycloruthenated triphenyl phosphite complex as the catalyst and KOPh as a transesterification co-catalyst (see below). It did not take long until it was noted that cyclometallation could also occur with other phosphane-containing hydridoruthenium(II) complexes. Ruthenacycles arising from internal C–H bond activation at a Ph_3P ligand in $[(Ph_3P)_3RuHCl]$ were found by James et al.[21] to be the main organometallic products of the stoichiometric hydrogenation of olefins, again being able to revert to the starting complex upon treatment with H_2. Similar observations were made by Stolzenberg and Muetterties who investigated the role of the ruthenacycle in the catalytic hydrogenation of alkynes.[22] The latter authors nonetheless concluded that the ruthenacycle was not a key intermediate in the hydrogenation itself. The same class of phosphite-containing ruthenacycles were also found to form in significant amounts in the catalyzed polymerization of ethylene and other olefins;[23] they were found to enhance considerably the catalytic hydrogenation of olefins.[24] The propensity of phosphite to undergo cycloruthenation was also outlined by Singleton and Hough in 1972, who pointed out the high reactivity of cationic diene ruthenium complexes reportedly yielding a bis-chelated Ru^{II} complex.[25]



Scheme 4. Cycloruthenation of triphenyl phosphite by a chloridohydridoruthenium complex.

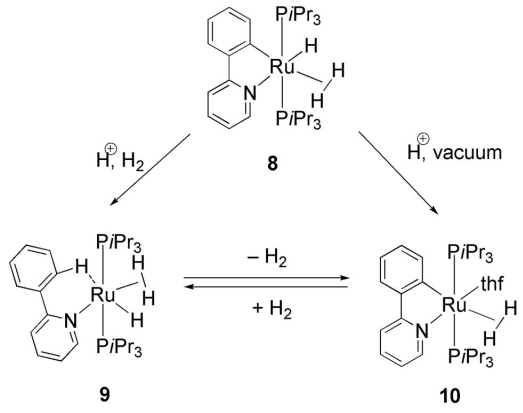
Polyhydrides such as $RuH_2(H_2)_2(PCy_3)_2$, synthesized from [Ru(cot)(cod)] by Chaudret and Poilblanc,[26] proved to be active in the cycloruthenation of PCy_3. In the cases of 2-phenylpyridine, benzoquinoline and 1-phenylpyrazole, Sabo-Etienne, Chaudret et al. used $RuH_2(H_2)_2[P(iPr)_3]_2$ as the metallation agent (compounds **7a**–**c**, Scheme 5).[27] These results are somewhat reminiscent of the first claims made by Wilkinson and Cole-Hamilton in 1977 as to the capability of $RuH_2(PPh_3)_4$ to reportedly operate the cycloruthenation of benzophenone.[28]



Scheme 5. Cycloruthenation of various aromatic ligands by means of a polyhydride generated from a coordinatively labile Ru^0 substrate.

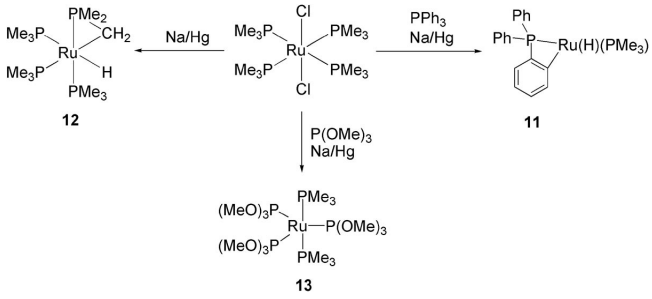
Recently, Sabo-Etienne et al. isolated a so-called C–H–Ru agostic species presented as the key intermediate in the aforementioned cycloruthenation reactions based on C–H bond activation.[12] The authors outlined the formal reversibility of the cyclometallation: cycloruthenated complex **8** was able to revert to agostic intermediate **9** upon exposure to acid and H_2 (Scheme 6). Computational investigations and ^1H NMR spectroscopic line shape analysis led to an estimated value of the intrinsic agostic interaction energy of ca. 16 kJ mol^{-1}.

According to Werner, *trans*-$RuCl_2(PMe_3)_4$ was found to cyclometallate triphenylphosphane to give **11**, under reductive conditions, by a mechanism involving the transient formation of a Ru^0 species, which was trapped by coordination of $P(OMe)_3$ to give **13** (Scheme 7).[29] In the absence of PPh_3, the reduction of *trans*-$RuCl_2(PMe_3)_4$ would yield a three-membered ruthenacyclic product, **12**, resulting from



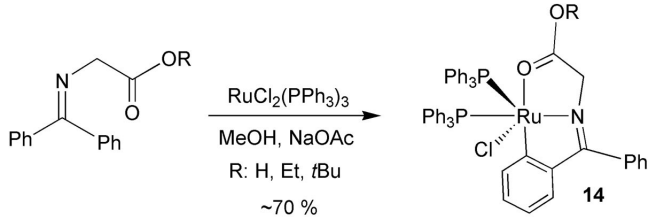
Scheme 6. The reversibility of cycloruthenation of **8** in acidic conditions.

the oxidative addition of the Ru^0 centre at a C–H bond of a methyl group of a Ru-bound PMe_3 ligand.



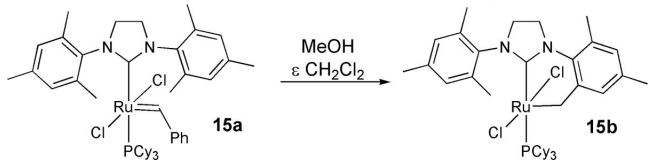
Scheme 7. Cycloruthenation by C–H bond activation with intermediary Ru^0 species generated by reduction over sodium–mercury amalgam.

Worthy of note is the capability of $RuCl_2(PPh_3)_3$ to cyclometallate so-called "O'Donnell Schiff bases" such as diphenylmethylene glycine ester, the latter behaving as a tridentate ligand in **14** (Scheme 8),[30] and to efficiently cyclometallate PCP ligands as reported by van Koten et al.[15] and Fogg et al.[31]



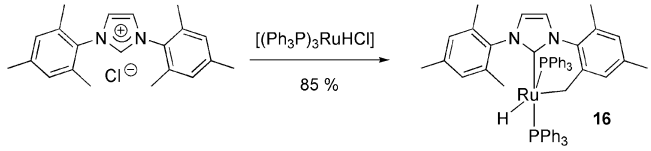
Scheme 8. A typical example of cycloruthenation by using $RuCl_2(PPh_3)_3$.

N-heterocyclic carbenes can also be subject to cycloruthenation, a rather undesired process in many cases. Grubbs et al.[32] figured that **15a** (Scheme 9) was unstable in methanol solutions containing minute amounts of CH_2Cl_2. At room temperature, this complex would readily convert into **15b**, with loss of the benzylidene fragment (Scheme 9).



Scheme 9. Incidental cycloruthenation of a Ru–NHC carbene complex.

Morris et al. provided convergent results as to the tendency of electron-deficient Ru^{II} complexes to favour C–H bond cleavage and cyclometallation with any proximal C–H bond located in close vicinity to the Ru centre.[33] For instance, the treatment of $[(Ph_3P)_3RuHCl]$ with dimesitylimidazolium chlorides yields essentially ruthenacycle **16**, which results virtually from oxidative addition at Ru^0 of one C–H bond of a mesityl methyl group (Scheme 10).



Scheme 10. Incidental cycloruthenation of *N*,*N*-bis(mesitylimidazolium) by a chloridohydridoruthenium complex.

Ruthenium Chelates

Bis(2,2′-bipyridine) and terpyridine ruthenium complexes have been under scrutiny in quite a large number of articles, because of the physical properties induced by the presence of the π-accepting chelating motif (vide infra). Most authors concluded that, for the cyclometallation of such cluttered chelate complexes to occur efficiently, the creation of a greatly electrophilic ruthenium centre was required. To achieve this, the formation of cationic solvates upon removal of chlorido ligands [with silver(I) salts for instance] was advocated in most cases.

This is particularly true for all the cycloruthenation reactions of 2-arylpyridines considered with *cis*-$[(bpy)_2RuCl_2]$ (**17**) (Figure 3) derivatives[34–36] and for similar complexes bearing a Ru-bound aminocarbene ligand.[37]

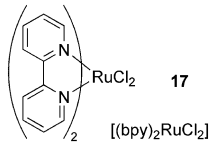
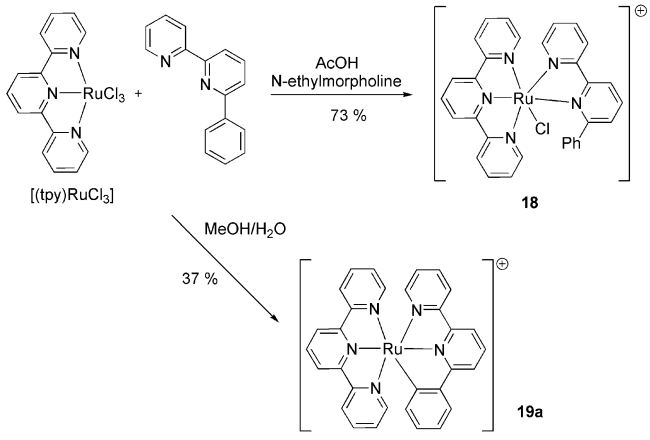


Figure 3. Dichloridobis(bipyridine)ruthenium **17**.

With ruthenium(III) complex $[(tpy)RuCl_3]$, the removal of all the chlorido ligands is an even more acute issue, a difficulty to be added to the fact that the ruthenium centre undergoes a formal reduction from oxidation state +3 to +2, a prerequisite for the C–H bond cleavage to occur as pointed out by Thummel.[38] Constable et al. have shown that the fate of the reaction of $[(tpy)RuCl_3]$ with 6-aryl-2,2′-bipyridines depends essentially on the choice of the polar-protic solvent with the right dielectric constant.[36,39] For

instance, the use of a mixture of acetic acid and *N*-ethylmorpholine would yield the chloridoruthenium(II) coordination adduct **18** in 73% yield, whereas in a 5:1 mixture of methanol and water the ruthenacycle would be produced in 37% yield (Scheme 11).



Scheme 11. Influence of the nature of the solvent on the ruthenation of 6-phenyl-2,2′-bipyridine by (tpy)$RuCl_3$.

Similar conclusions as to the relevance of the choice of solvent were made by Cargill Thompson, Ward et al. for the cycloruthenations of various *N*-methyl terpyridinium ligands by [(tpy)$RuCl_3$].[40] Steel et al. reported similar cases of cyclometallation of tritopic pyrazolylmethylbenzenes with [(tpy)$RuCl_3$][41] and even observed spectroscopically what could be the C–H···Ru *agostic* intermediate **20** formed prior to C–H bond activation by the Ru^{II} centre (Figure 4), a species somewhat reminiscent of the one isolated by van Koten et al. with a slightly different system of ligands and involved in so-called "transcyclometallation" reactions (vide infra).[42]

A rare case of reversible and pH-dependent cycloruthenation of 6-(2-thienyl)-2,2′-bipyridine with [(tpy)$RuCl_3$] was reported by Constable et al. (Scheme 12).[43] The authors

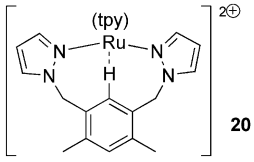
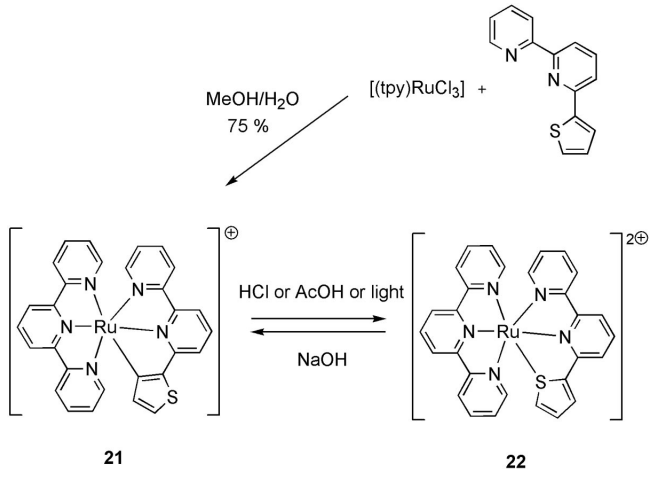


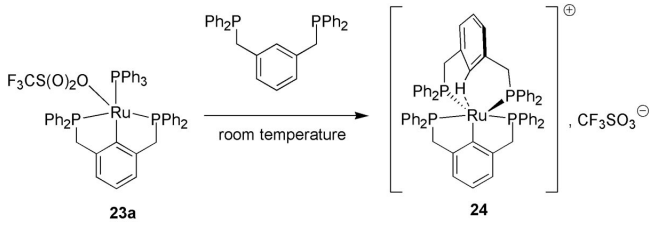
Figure 4. Agostic intermediate arising from the reaction of (tpy)$RuCl_3$ with a dipyrazolymethylbenzene derivative.

demonstrated that ruthenacycle **21**, formed in 75% yield in a 9:1 mixture of methanol/water, could produce a N,N,S bonded adduct **22** upon treatment with acid or exposure to light, this process being reversed upon reaction with aqueous NaOH.



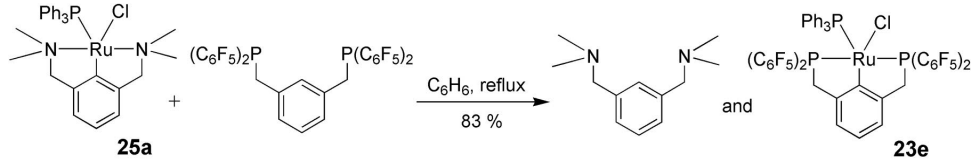
Scheme 12. Sensitivity of complex **21** to the relative acidity of the medium.

Ruthenium chelates containing a pincer-type ligand may undergo ligand exchange, or *transcyclometallation*, upon treatment with a different pincer ligand: van Koten et al. have evidenced the mediacy of an agostic intermediate **24**, which was isolated and structurally characterized (Scheme 13).[42]



Scheme 13. Formation of complex **24**, a key intermediate in the transcycloruthenation reaction.

This methodology was applied to the synthesis of **23e**, a ruthenacycle of a highly fluorinated PCP pincer ligand, by reacting a NCN Ru^{II} substrate, **25a**, with the free PCP ligand in boiling benzene (Scheme 14).[44]

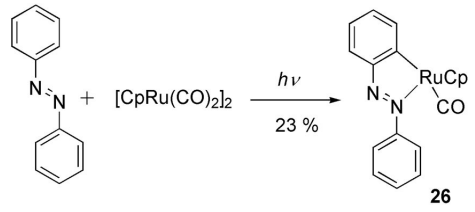


Scheme 14. Example of transcycloruthenation according to van Koten et al.

Pseudo-Tetrahedral Ruthenium Complexes

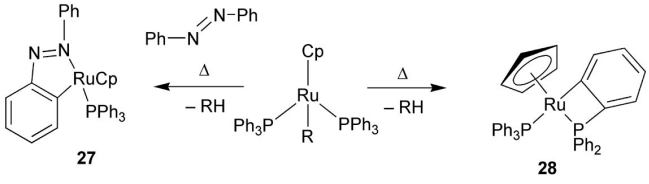
It is always worth recalling that in pseudo-tetrahedral complexes the metal centre is basically located in an octahedral coordination environment. However, it may be generally more convenient to consider this class of compounds as virtually tetrahedral, as three coordination sites are engaged in a polyhapto interaction with a somewhat spectator aromatic ligand such as η^6-arenes or η^5-cyclopentadienyls. In most cases the ruthenium centre is stereogenic, and most starting cyclometallation reagents are prochiral if not chiral. This feature, also shared with all – strictly speaking – octahedral complexes, introduces a challenging issue especially if chiral or prochiral ligands are considered in cyclometallation reactions, as diastereomeric mixtures of products may form. The presence of a spectator η^5- or η^6-bonded ligand introduces strains of both steric and electronic nature, which surely impact on the fate of the cyclometallation process.

In 1970, Bruce, Iqbal and Stone reported the cycloruthenation of azobenzene by $[CpRu(CO)_2]_2$, which happened to occur only upon irradiation with UV light and not upon heating (compound **26**, Scheme 15).[45] Much later, Kisch et al. confirmed the importance of activation by light for a similar reaction between azobenzene and $[Cp^*Ru(CO)_2]_2$.[46]



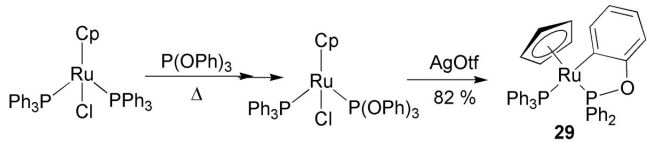
Scheme 15. Light-promoted cycloruthenation of azobenzene.

The use of (alkyl) or (aryl)(cyclopentadienyl)ruthenium complexes was also envisaged to ease cycloruthenation reactions based on C–H bond action. Stone et al.[47] and later Kisch et al.[46] reported the cycloruthenation of azobenzenes by $[CpRu(PPh_3)_2R]$ and $[Cp^*Ru(CO)_2(Me)]$, respectively. The former complex reportedly produced a cycloruthenated azobenzene, **27**, after thermolytic treatment, whereas the latter required a preliminary activation by irradiation to enable the C–H bond activation step (Scheme 16). In the absence of any exogenous ligand, $[CpRu(PPh_3)_2R]$ would convert to **28**.



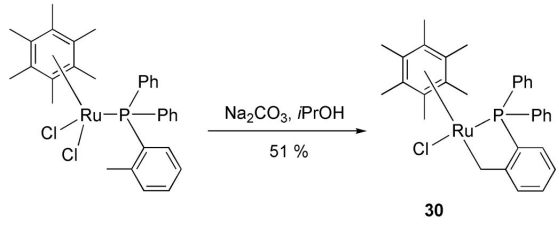
Scheme 16. Alkylcyclopentadienylruthenium complexes as metallating agents.

Quite interestingly, Roundhill et al.[48] noted that the removal of a chlorido ligand by silver(I) salts could readily trigger cycloruthenation in coordinatively saturated substrates (product **29**, Scheme 17). However, the authors were not able "to differentiate between a pathway involving oxidative addition at Ru^{II} or electrophilic attack by the cationic metal centre". Evidence for the oxidative addition path was provided earlier by Werner et al. with an electron-deficient (η^6-benzene)Ru species.[49]



Scheme 17. Ag^+-triggered cycloruthenation of triphenyl phosphite.

In an attempt to prepare a hydridoruthenium species from the dichlorido(η^6-arene)(diphenyl-*ortho*-tolylphosphane)ruthenium substrate, Bennett and Latten uncovered a quite intriguing cycloruthenation reaction involving C–H bond activation at the *ortho*-methyl substituent of the Ru-bound phosphane ligand (compound **30**, Scheme 18).[50] In this case a hydridoruthenium intermediate, which formed upon hydrogen atom transfer from 2-propanol, was proposed.

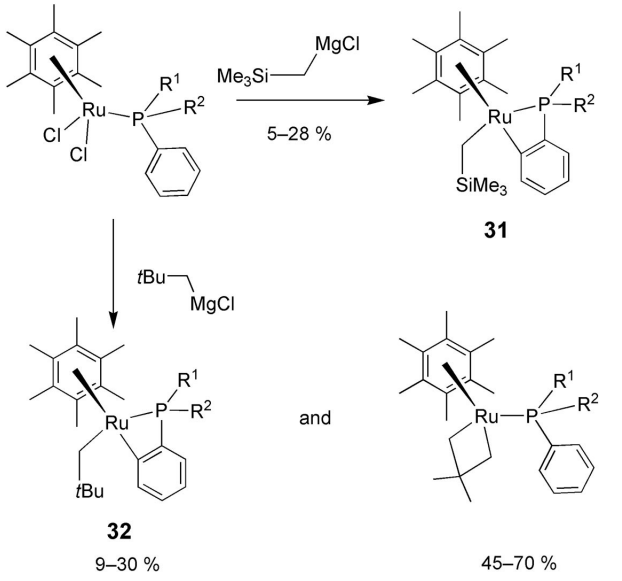


Scheme 18. Incidental cycloruthenation under hydrogen-atom-transfer conditions.

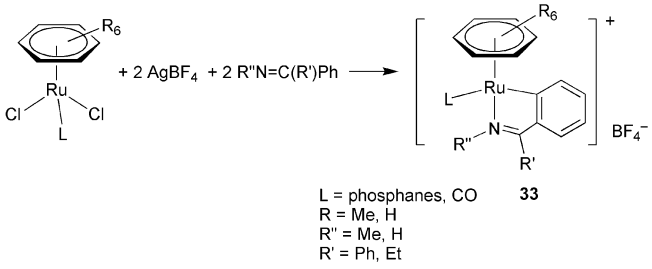
Other cycloruthenations of Ru-bound phosphanes triggered by the formation of transient alkyl–ruthenium species putatively formed upon reaction of a dichlorido(η^6-arene)-(aryldialkylphosphane)ruthenium substrate with alkylmagnesium reagents were reported by Diversi et al. (compounds **31** and **32**, Scheme 19).[51,52]

(η^6-Arene)ruthenium derivatives have been shown to lead to successful cyclometallation reactions with a large variety of nitrogen-containing ligands (Scheme 20). Boncella et al.[53] first showed that imine ligands could be cycloruthenated when reacted with these precursors. Till then, it was shown that this starting material was quite helpful in providing successful cycloruthenation with a large variety of N-containing ligands. The use of silver salts was, however, shown to be unnecessary, as KPF_6 led to the same effect.[54–59]

A closely related reaction was performed by Davies et al., who found that imines could be cycloruthenated by $[(\eta^6\text{-}p\text{-cymene})RuCl_2]_2$, but the absence of either potassium or silver salts led to a neutral chloride-containing compound.[60] Of particular usefulness were primary and secondary ben-

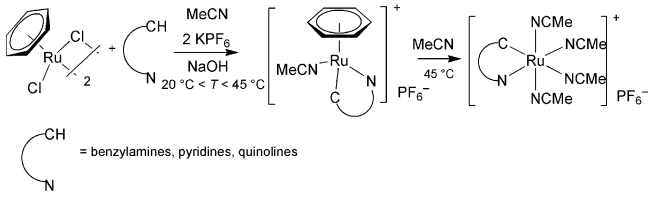


Scheme 19. Grignard reagents as promoters of cycloruthenation.



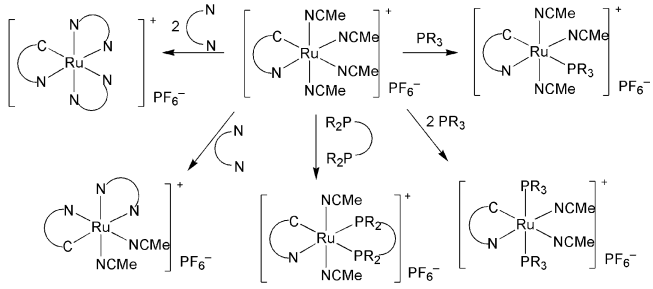
Scheme 20. Cycloruthenation of imines by (η^6-arene)ruthenium derivatives.

zylamine derivatives (Scheme 21), which were very readily cycloruthenated, leading thus to potent catalyst precursors for the reduction of ketones and imines by H-transfer reactions (see below).



Scheme 21. Generalization of the cycloruthenation using (η^6-benzene)ruthenium dichloride dimer.

These (η^6-arene)dichloridoruthenium dimers were also successfully used to attain the metallation of other N-containing ligands such as pyridine or quinoline derivatives (see Scheme 21). In these cases, however, the η^6-benzene ligand was easily substituted by the acetonitrile ligand. The compounds thus formed were further used as starting materials to obtain cycloruthenated compounds with various ligands around the ruthenium atom (Scheme 22). These latter molecules display interesting properties, as they were shown to be efficient redox mediators[56,57,61,62] or to have important biological effects[63](see below).



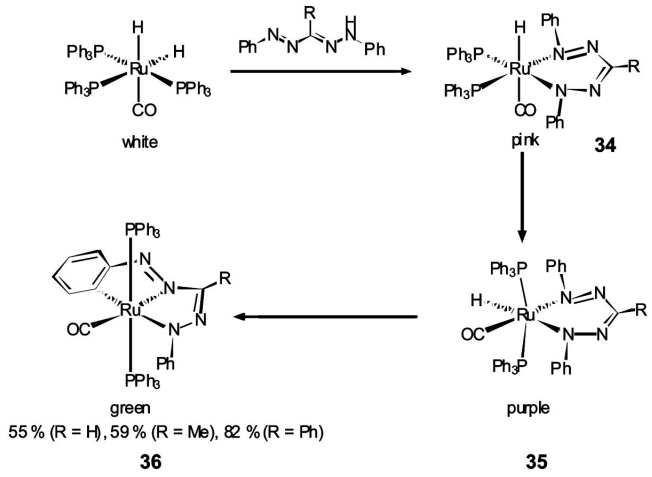
Scheme 22. Substitution reactions of acetonitriles by mono- and bidentate N- or P-containing ligands.

It was shown that the mechanism of the cycloruthenation with these arene–ruthenium complexes was best described as an electrophilic substitution of aromatics rather than a genuine C–H activation process. Indeed, when a series of substituted dimethylbenzylamine ligands were cycloruthenated, it was observed[55] that the phenyl rings substituted by electron-releasing groups, e.g. by one or two OMe units, were more readily cyclometallated than the corresponding substrates having an electron-attracting group such as a NO_2 substituent. The exact role of the base is not yet completely rationalized, and it is still a subject of further research. However, its presence was shown to be necessary, part of its role being to help the reaction by neutralizing the protons that evolve during the metallation process. It was also observed that $[(\eta^6\text{-benzene})RuCl_2]_2$ was the best starting material for obtaining the desired cycloruthenated derivatives, whereas $[(\eta^6\text{-}p\text{-cymene})RuCl_2]_2$ was sometimes found to be inefficient for this reaction involving benzylamines. This fact militates also in favour of an electrophilic substitution, as the Ru atom in the *p*-cymene derivative should be less electrophilic than that in the benzene-containing compound. Very recently, Arends et al.[64] succeeded in cyclometallating benzylamine with this latter starting material. However, the resulting compound (that displayed interesting catalytic activities, see below) was generated in situ, not isolated, and hence characterized only through its ^{1}H NMR spectrum.

Octahedral Mononuclear Carbonylruthenium Complexes

A great number of mononuclear carbonylruthenium complexes have been investigated in cycloruthenation reactions. Two main classes of compounds will be addressed herein, that is, on the one hand carbonylhydridoruthenium complexes, and on the other hand, carbonylhalidoruthenium complexes.

Ibers et al.[65] outlined the peculiar reactivity of both $RuCl(H)(CO)(PPh_3)_3$ and $Ru(H)_2(CO)(PPh_3)_3$ towards diphenylformazans, whereby it was established that one hydrido ligand acted as a base in the preliminary coordination step preceding *ortho*-ruthenation, of which the intermediates, i.e. **34**–**36**, were readily isolated and characterized by various spectroscopic techniques (Scheme 23).

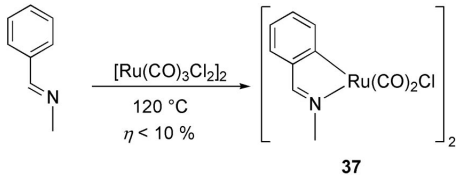


Scheme 23. Cycloruthenation of formazans.

A host of examples of ligand cycloruthenation by using either of the above-mentioned carbonylhydridoruthenium complexes and staging phosphites,[66] benzamides,[67] benzonitriles[68] and benzylideneamines[69] can be found in the literature.

Carbonylchloridoruthenium complexes such as $[Ru(CO)_3Cl_2]_2$ and $[Ru(CO)_2Cl_2]_n$ have received little attention. There are two types of ruthenium complexes containing the $Ru(CO)_2Cl_2$ motif. The first, a solvate generally formulated as $Ru(CO)_2Cl_2{\cdot}\mathbf{S}_2$ (**S** = solvent), is the main component of Chatt's "yellow solution" made by the reaction of $RuCl_3{\cdot}nH_2O$ with CO.[70] The second, $[Ru(CO)_2Cl_2]_n$, is reportedly a polymer that can be obtained from high-temperature vacuum desolvation of $Ru(CO)_2Cl_2{\cdot}\mathbf{S}_2$.

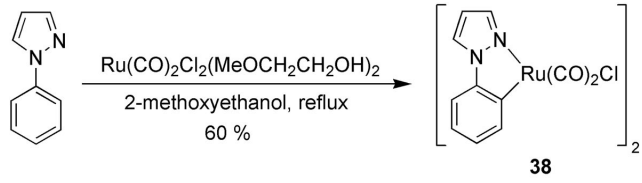
Cycloruthenation with $[Ru(CO)_3Cl_2]_2$ requires the departure of one carbonyl ligand, and therefore most authors used high temperature to initiate the reaction, albeit with moderate success. For instance, benzylidene(methyl)amine would convert only into minute amounts of the corresponding ruthenacycle **37** (Scheme 24).[71]



Scheme 24. Cycloruthenation of benzylidene(methyl)amine with bis(tricarbonyldichloridoruthenium).

To cope with this intrinsic relative inertness of $[Ru(CO)_3Cl_2]_2$, Bruce et al. introduced bases (Et_3N, NaO*i*Pr) into the reaction medium, which were expected to promote proton capture in the course of the cycloruthenation of azobenzene.[72] However, yields in cycloruthenated azobenzene[73] barely exceeded 25%. The authors finally found out that high yields relative to Ru (70%) could essentially be ensured by the use of a large excess of azobenzene "in the absence of any solvent".[72] Nonoyama et al. reported the cycloruthenation of 2-(*p*-toluidino)pyridine,[74] *N*,*N*-dimethylfuran-2(and 3)-carboselenamide[75] and *N*,*N*-dimethylbenzo[*b*]furan-2-carbothio(and seleno)amides[76] by treating the latter compounds with $[Ru(CO)_3Cl_2]_2$ in refluxing 2-methoxyethanol.

Hiraki et al. issued the first report on the use of $Ru(CO)_2Cl_2{\cdot}\mathbf{S}_2$ for the cycloruthenation of 1-phenylpyrazole (Scheme 25), 2-phenylpyridine and benzoquinoline in refluxing 2-methoxyethanol with yields spanning from 60 to 65%.[70] In the absence of any crystallographic structural information, they analyzed the normal modes of CO stretching vibrations of the isolated complexes and proposed structures **F** and **G** (Figure 5), based on these partial data, as the most plausible configurations for these dinuclear compounds.[70]



Scheme 25. Reaction of 1-phenylpyrazole with solvated dicarbonyldichloridoruthenium that results in the formation of **38**.

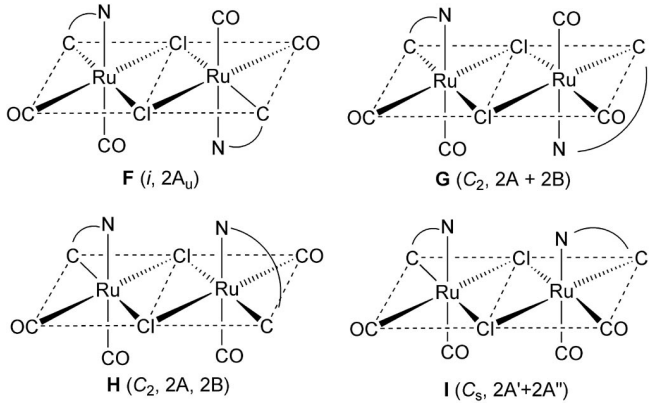
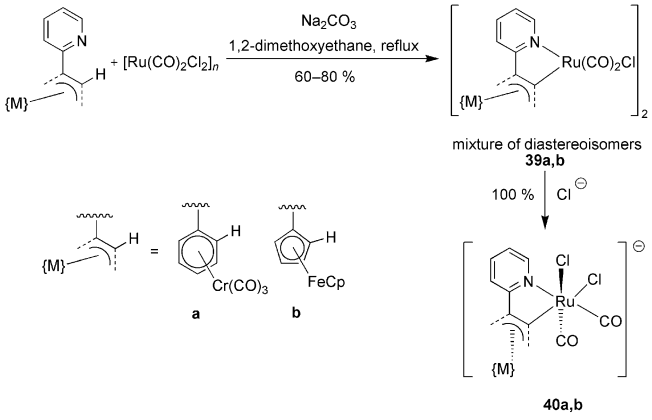


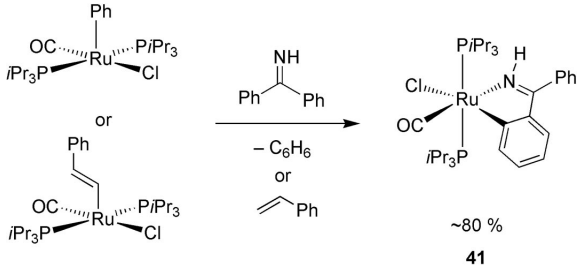
Figure 5. The four configurations of the di-μ-chlorido-bridged ruthenium complexes proposed by Hiraki et al.: only forms **F** and **G** were deemed reasonable to account for the IR spectra of the synthesized ruthenacycles.

Recently, some of us reported that planar prochiral ligands such as 2-ferrocenyl or 2-[(η^6-phenyl)tricarbonylchromium]pyridine could also undergo cycloruthenation upon reaction with $[Ru(CO)_2Cl_2]_n$ under mild conditions (80 °C) and with the help of a weak inorganic base, sodium carbonate (Scheme 26).[77] It was shown that under these conditions the reaction would lead to a rather complex mixture of μ-chlorido-bridged diastereoisomers **39a**,**b**, all possessing the same local configuration at the ruthenium centre. This was essentially demonstrated by converting the chlorido-bridged dimers **39a**,**b** into monomers **40a**,**b** by reaction with monodentate ligands or with a chloride salt.[78] It is noteworthy that tricarbonylchromium complexes of 2-phenyloxazoline and *N*,*N*-dimethylbenzylamine reportedly failed to undergo cycloruthenation.[78]



Scheme 26. The cycloruthenation of planar prochiral pyridine derivatives.

One should also note the rare cases of cycloruthenation of an imine by coordinatively unsaturated square-pyramidal phenyl– and styryl–Ru^{II} complexes reported by Esteruelas et al. (Scheme 27).[79] In this case the phenyl and styryl moieties play the formal role of internal bases, the release of the octahedral product **41** being accompanied by the formation of either benzene or styrene.

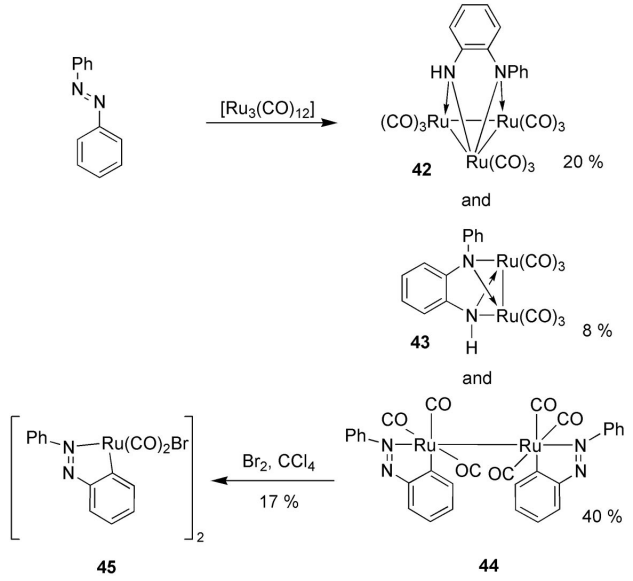


Scheme 27. Cycloruthenation of benzophenone imine by a square-pyramidal styryl– and phenyl–ruthenium complex.

Trinuclear Ruthenium Clusters and Dinuclear Carbonylruthenium Complexes

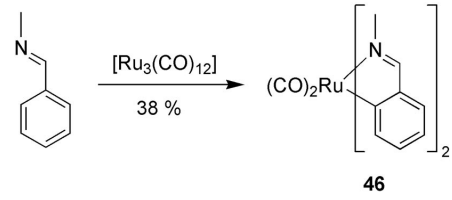
Thermolytic coupling of ruthenium(0) $Ru_3(CO)_{12}$ with ligands has been investigated in the early 1970s by many authors.[80,81] Nevertheless, it was found that the capability of $Ru_3(CO)_{12}$ to produce mononuclear bis-chelated $Ru(CO)_2$ species by C–H bond activation was counterbalanced by the somewhat unpredictable character of the mechanism of this thermolytic reaction, which would often lead to a significant array of trinuclear and dinuclear ruthenium cluster compounds as exemplified below (compounds **42**–**44**, Scheme 28) for a reaction between azobenzene and $Ru_3(CO)_{12}$.[82]

Ligands such as benzo[*h*]quinoline[83] and benzylidene(methyl)amine[71] (Scheme 29) may cleanly afford the corresponding bis-chelated *cis*-dicarbonylruthenium species such as **46**. However, generalization to other ligands and application of the same procedure to azobenzenes leads to trinuclear Ru clusters containing a semitidine bridging ligand produced by chemical degradation of the azobenzene



Scheme 28. Reactivity of azobenzene towards thermolytic treatment with dodecacarbonyltriruthenium.

substrate, the mechanism of which was disclosed by Bruce et al.[84]



Scheme 29. Cycloruthenation of benzylidene(methyl)amine.

There are only a few X-ray structures of bis-cycloruthenated compounds containing the $Ru(CO)_2$ core;[85,86] one of them (Figure 6) is disclosed here by the authors of the present review and was prepared in minute amounts by reaction of $Ru_3(CO)_{12}$ with 2-[tricarbonyl(η^6-phenyl)chromium]-3-methylpyridine.[87]

Other pyridine, polypyridine, quinoline, phosphane, polyphosphane or phosphite complexes of polynuclear carbonylruthenium clusters may undergo intramolecular cycloruthenation and yield compounds in which the organic moiety bridges two or three ruthenium centres.[88–98] These polynuclear compounds containing a cyclometallated unit are outside the scope of the present review and will not be further discussed here. To be noted, however, is the recent application of Klemperer's bis-cationic diruthenium complex, $[(MeCN)_6Ru_2(CO)_4]^{2+}$,[99] by Bera and Patra[100] to the cycloruthenation of 2-phenyl-1,8-naphthydrine. The reaction depicted in Scheme 30 provided an original agostic-cyclometallated compound **48**, in which one of the two naphthydrine moieties is cyclometallated whereas the other interacts through coordination of the nitrogen atoms and an agostic C–H···Ru interaction.

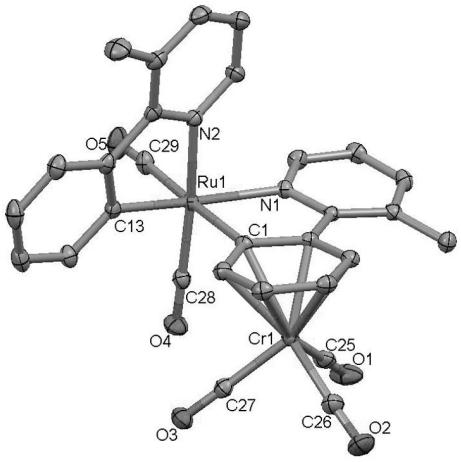
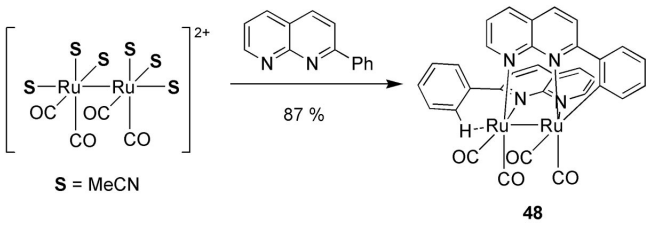


Figure 6. CSD mercury diagram of the molecular structure of compound **47**. This compound was formed in minute amounts by reaction of $Ru_3(CO)_{12}$ with 2-[tricarbonyl(η^6-phenyl)chromium]-3-methylpyridine in boiling toluene: the structure indicates the loss of one $Cr(CO)_3$ moiety during the thermolytic treatment. Selected interatomic distances in Å: Ru1–C28 1.876(3), Ru1–C29 1.920(3), Ru1–C13 2.052(2), Ru1–C1 2.100(2), Ru1–N2 2.133(2), Ru1–N1 2.170(2), Cr1–C1 2.298(2).



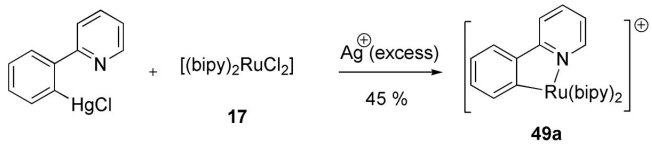
Scheme 30. *ortho*-Ruthenation of a phenylnaphthydrine.

2.2. The "C–M Activation" Route: Transmetallation by Ligand Exchange

The transmetallation reaction can be considered to be a reasonable alternative to the C–H bond activation route; it has been covered with a large array of ruthenium complexes. There have been reports essentially on the use of organomercury substrates and only in a few specific cases with organolithium substrates. As far as mercury(II) substrates are considered, two types of processes are found in the literature. The first, fully isohypsic from the point of view of the formal oxidation states at the metals, corresponds to a simple ligand exchange, whereby metals exchange their ligands. The second entails the formal reduction of the Hg^{II} substrate and the formation of metallic Hg^0 as byproduct.

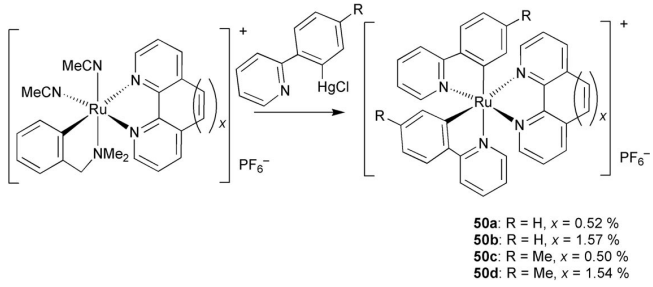
Transmetallation with Mercurated Ligands: Ligand Exchange

Transmetallation by ligand exchange requires available coordination sites at ruthenium. Constable et al.[101] reported that the reaction of bis(bipyridine)ruthenium(II) complex **17** with chloridomercurated 2-phenylpyridine to produce **49a** was possible only upon activation by removal of the chlorido ligands with silver salts (Scheme 31).



Scheme 31. Ag^+-assisted transmetallation according to Constable et al.

Homoleptic bis-chelated Ru^{III} complexes **50** were similarly prepared by Ryabov et al.[102] starting from bis(solvato) cyclometallated complexes of Ru^{II} and a chloridomercurated derivative of 2-phenylpyridine (Scheme 32): oxidation of the metal centre to the +3 oxidation states was caused by the inherent low Ru^{II}/Ru^{III} oxidation potential (from –0.21 to –0.25 V vs. SCE) of tris-chelated Ru^{II} species. It must be outlined that this method is the *second known to date* for the preparation of homoleptic *OC*-6 bisruthenacycles.

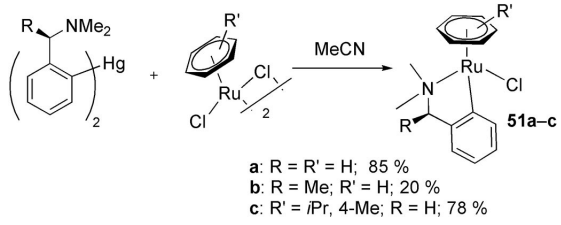


Scheme 32. Synthesis of homoleptic bisruthenacycles by transmetallation.

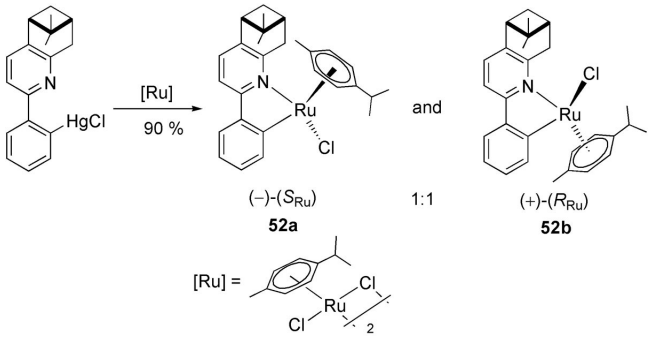
(η^6-Arene)ruthenium dichlorido dimers have been used by Pfeffer, Nelson[54,103,104] and by Chakravarty[105] for the synthesis of a host of half-sandwich cycloruthenated complexes with benzylamine, arylpyridine and diazobenzene derivatives (compounds **51a**–**c**, Scheme 33). The ligand-exchange reaction is sensitive to steric hindrance in the immediate vicinity of the reaction centre. With α-methylated benzylamine derivatives, the transmetallation yields highly unbalanced mixtures of diastereoisomers, which were shown to be "configurationally labile" at the metal centre.[106–109]

With chiral chloridomercurated 2-phenylpyridine, such as the one derived from 2-phenyl-5,6-pinenopyridine, the ligand-exchange reaction (Scheme 34) led to an equimolar mixture of diastereomers (–)-**52a** and (+)-**52b** that displayed high conformational persistence in polar solvents.[109] It is worthy to note that both isolated diastereomers displayed conformational instability in the presence of $HgCl_2$.

With chloridomercurated (η^6-arene)tricarbonylchromium substrates *rac*-**53** and *rac*-**56**, the well-known *stereoelectronic control* operated by the $Cr(CO)_3$ moiety was found to be responsible for the high diastereoselectivity of the li-

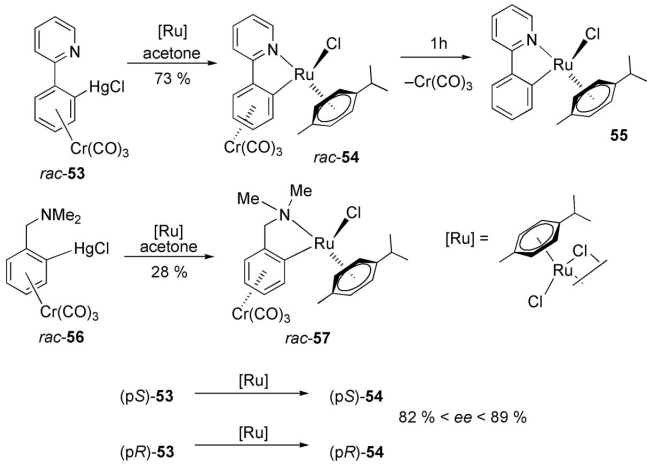


Scheme 33. Cycloruthenation by transmetallation of symmetric *N*,*N*-dimethylbenzylamine mercurials.



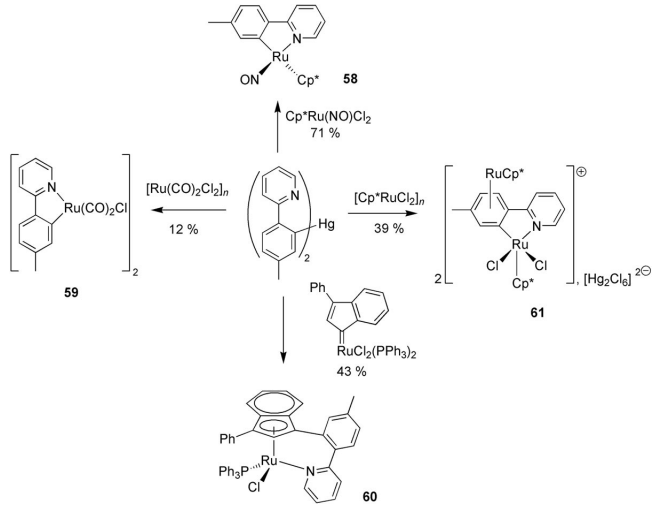
Scheme 34. Cycloruthenation of 2-phenyl-5,6-pinenopyridine by transmetallation of the chloridomercurated derivative.

gand-exchange reaction.[110] In two cases, i.e. *rac*-**54** and *rac*-**57**, it was demonstrated that the preferred relative configuration of the ruthenium centre in the final products would be that with the chlorido ligand *anti* with respect to the $Cr(CO)_3$ moiety (Scheme 35). This specificity was applied, starting from nonracemic chloridomercurated **53**, to the synthesis of p*S* and p*R* enantiomers of **54**, whose enantiopurity was assessed by using Lacour's BINPHAT salt as ^{1}H NMR chiral shift reagent.[110]



Scheme 35. Transmetallation as an efficient way to transfer Ru with relative retention of configuration.

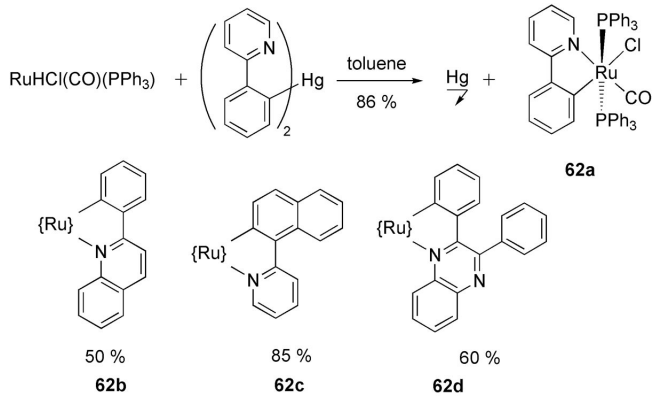
Leung et al. extended the ligand-exchange reaction to four additional ruthenium(II) complexes with yields ranging from moderate to good (compounds **58**–**61**, Scheme 36).[85] In the case of an alkylideneruthenium complex, the reaction with bis[2-(*p*-tolyl)pyridine]mercury led to an unexpected (η^5-indenyl)ruthenium(II) derivative, **60**, most probably resulting from the insertion of the alkylidene moiety into the C–Ru bond of the initially targeted ruthenacycle. With $[Cp^*RuCl_2]_n$ the transmetallation reaction was reportedly accompanied by the π-coordination of the "Cp*Ru" moiety to the tolyl fragment and with the formal oxidation of one Ru atom from formal state +2 to +4, thus affording a rare case of cationic planar-chiral cycloruthenated (η^6-arene)RuCp* complex, **61**.



Scheme 36. The reactivity of four different types of Ru reagents towards mercurated 2-phenylpyridine.

Transmetallation with Mercurated Ligands: Reductive Ligand Exchange

Hydridoruthenium complex $RuHCl(CO)(PPh_3)_3$ was found by Roper et al. to react readily with mercurated arylazines,[111,112] aryldiazines[112] and arylphosphanes,[113] producing the resulting *OC*-6 ruthenacycles and metallic mercury as a byproduct (compounds **62a**–**d**, Scheme 37). The conditions used for these reactions (reflux of toluene) suggest that the hydrido ligand contributed in the reduction of Hg^{II}.

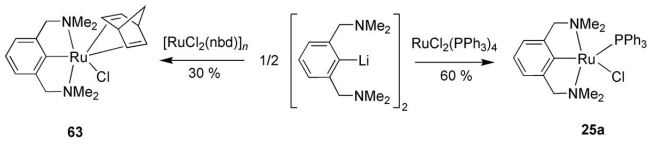


Scheme 37. Reductive ligand exchange using hydrido ruthenium species.

Similar cycloruthenation reactions with mercurated azobenzene derivatives and involving $RuHCl(CO)(PPh_3)_3$[114] and $RuHCl(CS)(PPh_3)_3$[115] were also reported by Flower et al.

Transmetallation with Lithiated Ligands

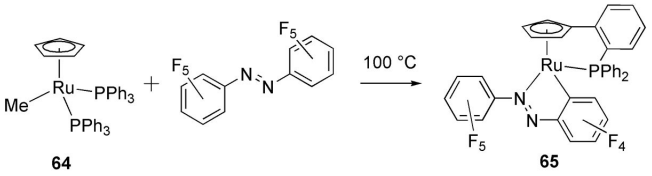
Whenever necessary, recourse to organolithium reagents proved to be rewarding: van Koten et al.[116] demonstrated that a lithiated pincer ligand could readily undergo transmetallation with Ru^{II} complexes of norbornadiene or triphenylphosphane with yields ranging from 30 to 60% (compounds **63** and **25a**, Scheme 38).



Scheme 38. Synthesis of pincer ruthenium complexes by transmetallation of a lithiated pincer ligand.

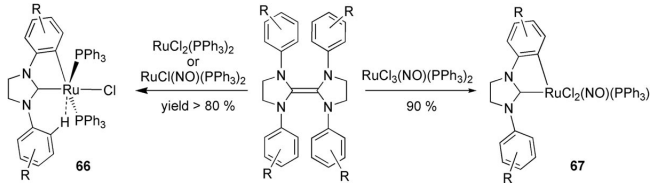
2.3. The "C–Y" Route: Isolated Cases of Cycloruthenation by Carbon–Element Bond Cleavage

To date, not much is known about the capability of ruthenium complexes to produce ruthenacycles by C–F bond cleavage. In the early 1970s, Stone et al. produced a short report of such a transformation involving $CpRu(Me)(PPh_3)_2$ and decafluoroazobenzene (Scheme 39).[117] The reaction, which was carried out at 100 °C under conditions similar to those used for the cycloruthenation of azobenzene,[47] produced compound **65**. The formation of this compound, the structure of which was elucidated thanks to X-ray diffraction analysis, entails a multifaceted process that includes C–H bond activation at the cyclopentadienyl ligand and the triphenylphosphane, C–C coupling and C–F bond activation at decafluoroazobenzene. Shortly afterwards, other attempts of cycloruthenation[118] with penta- and decafluoroazobenzene were made by the same group by using $Ru_3(CO)_{12}$ as the metallating agent and resulted in nothing else but the corresponding fluorinated (*o*-semitidine)$Ru_3(CO)_9$ derivatives (vide supra).



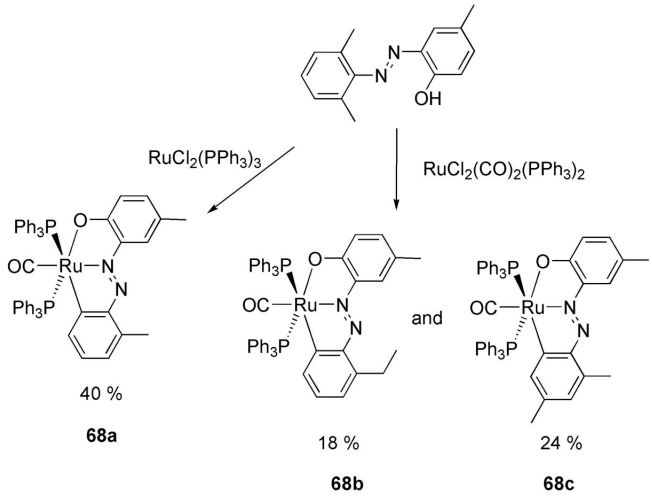
Scheme 39. C–F bond activation at perfluorinated azobenzene.

In their series of studies of the reactivity of electron-rich tetraaminoalkenes vs. transition-metal complexes, Lappert et al. reported that tetra-*N*-*para*-tolylbis(imidazolidinylidene) reacts with $RuCl_2(PPh_3)_3$ to afford a new pentacoordinate monocarbene ruthenium complex in 95% yield under thermolytic conditions.[119] The structure of this compound was deduced from that of its bis(triethylphosphane) analogue. The structure of the latter indicated that the ruthenium sits in a square-pyramidal environment and that a hydrogen atom of a proximal tolyl fragment virtually occupies the sixth free position of coordination of the metal centre. Similar complexes, **66** and **67**, were obtained by C–C bond cleavage by subjecting other tetra-*N*-arylbis(imidazolidinylidene) compounds to reaction with $RuCl(NO)(PPh_3)_2$ and $RuCl_3(NO)(PPh_3)_2$ (Scheme 40).[120] Worthy to be noted is the NO displacement occurring upon formation of the ruthenacycle with $RuCl(NO)(PPh_3)_2$.



Scheme 40. C–C bond activation and cycloruthenation of "electron-rich" alkenes.

Other cases of cycloruthenation involving the cleavage of C–C bonds have been reported by Bhattacharya et al. in reactions staging $RuCl_2(PPh_3)_3$ or $RuCl_2(CO)_2(PPh_3)_2$ and hydroxy- and methyl-substituted azobenzenes (Scheme 38). With the former complex,[121] the product, **68a**, is an octahedral aryloxidocarbonylruthenium(II) complex. As revealed by experimental evidence, the CO ligand results from an oxidative extrusion of one of the *ortho*-methyl groups located in close vicinity to the Ru^{II} centre. With the latter complex,[122] two products resulting from a formal *methylotropism* (**68b** and **68c**, Scheme 41) were isolated with an overall yield of 42%.

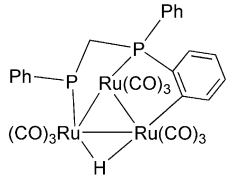


Scheme 41. Methylotropism in the cycloruthenation of hydroxy- and methyl-substituted azobenzenes.

Unusual cases of decarbonylative cycloruthenation of aromatic aldehydes were reported by Chakravorty et al. in reactions staging $RuCl_2(PPh_3)_3$ and a series of salicylalde-

hydes in the presence of a primary amine: products consisting of an octahedral carbonylphenolatoruthenium complex[123] were isolated.

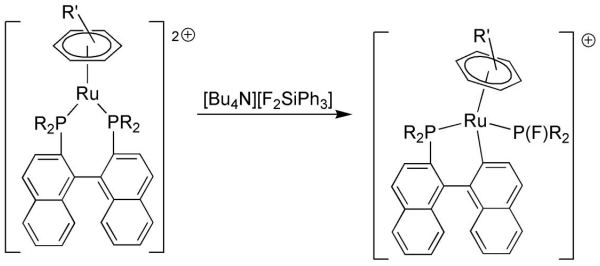
Evidence for spontaneous cycloruthenation occurring upon C–P bond cleavage has been reported by Bruce for the thermolysis of $Ru_3(\mu\text{-dppm})(CO)_{10}$, (dppm = diphenylphosphanylmethane) which affords a new Ru_3 cluster, **69**, containing a μ-hydrido ligand and a large fragment of the rearranged bis(diphenylphosphanyl)methane ligand (Figure 7).[124] The reader should also refer to other similar findings by Puddephatt et al. with dinuclear carbonylruthenium complexes of dppm.[125]



69

Figure 7. The product of the thermolysis of $Ru_3(\mu\text{-dppm})(CO)_{10}$.

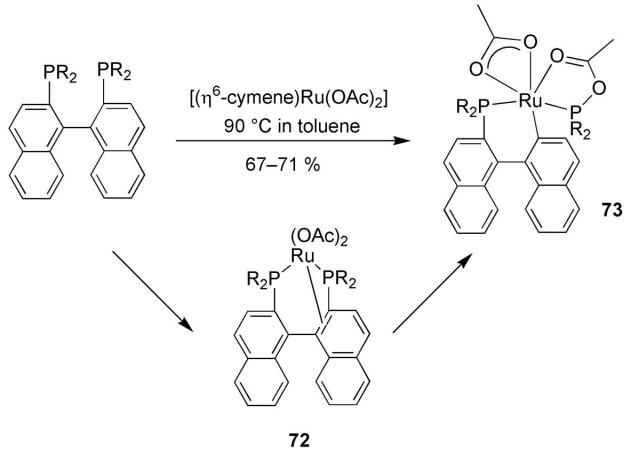
Recent examples of C–P bond cleavage by mononuclear Ru^{II} species have been reported by Pregosin et al. for BINAP-type ligands. The first case mentioned here (Scheme 42)[126] is a C–P cleavage induced by the $F_2SiPh_3^-$ anion at low temperature with dicationic BINAP chelates of (η^6-arene)Ru, which reportedly resulted in the formation of an electron-saturated pseudo-tetrahedral complex, **71**.



70 **71**

Scheme 42. Fluoride-promoted C–P bond cleavage and cycloruthenation of BINAP.

A second case[127] was that occurring in the reaction of a BINAP ligand (compound **73**, Scheme 43) with [(η^6-cymene)$Ru(OAc)_2$] at 90 °C in toluene. The authors, who initially intended to prepare a Ru^{II} complex bound to a conventional (P,P)-chelate, concluded, on the basis of ^{31}P NMR spectroscopic evidence, that the C–P bond cleavage was most probably preceded by the η^2 coordination of the Ru centre to one of the naphthyl fragments of the BINAP ligand (compound **72**, Scheme 43). The corresponding ruthenacycles were obtained in reasonable yields, and the structure of one of them was established by X-ray diffraction analysis.



73 **72**

Scheme 43. C–P bond activation and cycloruthenation of BINAP derivatives.

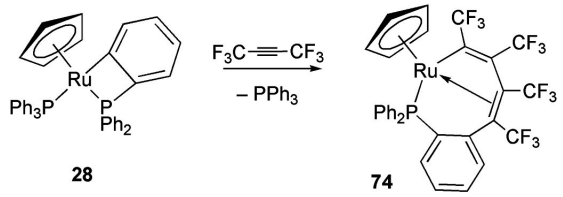
3. Reactivity of the Cycloruthenated Unit

As cyclometallated compounds were, and still are, considered to be intermediates in the C–H activation reaction, obvious reactivity studies that were first carried out were reactions involving the M–C bond of the cyclometallated species, especially those leading to the formation of C–C bonds. However, in this section the "organic" C–H activation processes that take advantage of the presence of a directing atom on a given substrate to afford catalytic C–C bond formation and in which the metallacyclic unit is not observable will not be discussed, despite the fact that these reactions usually involve cyclometallated species.[128] Reactions leading to C–C or C–heteroatom bond formation have been indeed achieved for palladium compounds with various reagents, as many papers were published involving stoichiometric amounts of the palladium species.[129–132] Related studies were, however, much less frequently performed with the corresponding cycloruthenated compounds.

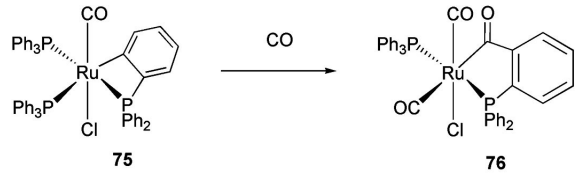
3.1. Addition of Unsaturated Substrates onto Cycloruthenated Compounds

One of the earliest examples we are aware of was reported by Bruce and Stone,[133] who found that hexafluorobut-2-yne could be inserted twice into the Ru–C bond of a cycloruthenated triphenylphosphane, thus releasing the somewhat tense four-membered metallacyclic ring of *ortho*-ruthenated triphenylphosphane in the starting material to form an eight-membered ring involving the metal (Scheme 44). Characterization of the product was based on ^{19}F NMR spectroscopic data, which provided evidence that all CF_3 groups were *cis* to each other. Unfortunately no X-ray diffraction analysis is available.

A classical example of CO migration in a related *ortho*-ruthenated triphenylphosphane compound was reported by Bennett et al. (Scheme 45).[113] The four-membered ring of the corresponding osmium derivative was inert under the same reaction conditions, and all efforts to induce CO insertion into the Os–C bond failed.

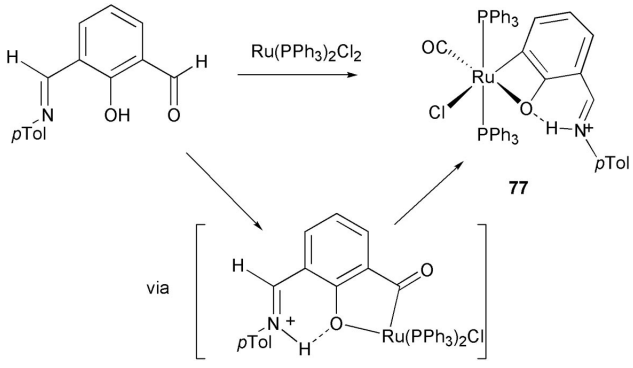


Scheme 44. Insertion of hexafluorobut-2-yne into the Ru–C bond of *ortho*-ruthenated PPh_3.



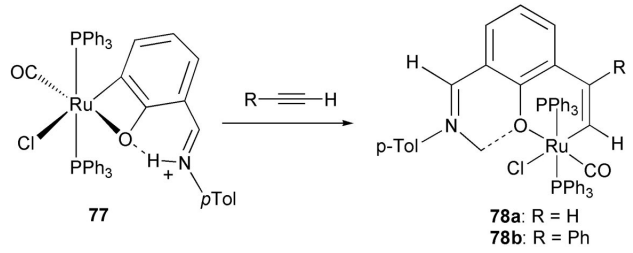
Scheme 45. CO migration into the Ru–C bond of a four-membered cyclometallated unit.

Decarbonylation of diformylphenol Schiff bases was found to occur, affording rare four-membered ruthenacycles in which an oxygen atom of the phenol unit is found to be the donor atom (Scheme 46).[134,135]



Scheme 46. Decarbonylation of diformylphenol to afford a four-membered ruthenacycle.

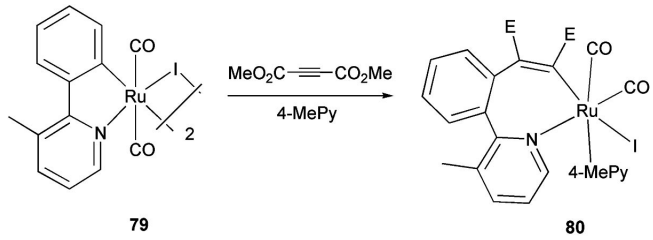
The Ru–C bond of the thus obtained ruthenated four-membered ring was quite reactive with alkynes (Scheme 47), as the insertion of either acetylene or phenylacetylene was readily observed.[136]



Scheme 47. Insertion of alkynes into a Ru–C bond affording a six-membered metallacycle.

It was believed that the alkyne insertion, which is highly regioselective for the unsymmetrical phenylpropyne, occurs by coordination of the alkyne on the ruthenium centre, this process taking place by the initial cleavage of the O–Ru bond of the four-membered ruthenacycle of **77**.

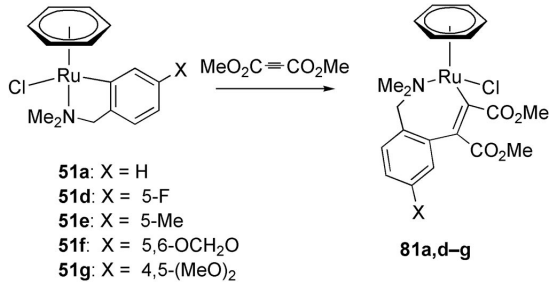
Alkyne insertion into the Ru–C bond of cycloruthenated species obtained with N-containing ligands and leading to stable organometallics was shown to occur (Scheme 48).[137] Activated alkynes such as dimethyl acetylenedicarboxylate (DMAD) led to insertion into the Ru–C bond of *ortho*-ruthenated 2-phenylpyridine, affording a ruthenated seven-membered ring that was characterized by X-ray diffraction studies.



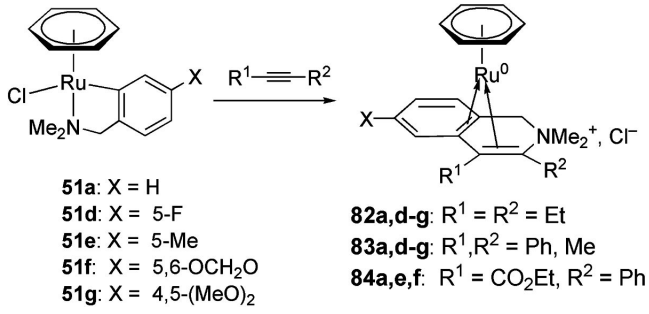
Scheme 48. Formation of a seven-membered ring by insertion of alkyne into metallated phenylpyridine.

At about the same time, this group found that this reaction could also be performed with cycloruthenated compounds built up from *N*,*N*-dimethylbenzylamine derivatives having a different structure than **79**.[54,138]

The corresponding compounds having *para*-cymene instead of a benzene η^6-capping ligand on the ruthenium atom led to the same type of products.[138] When the reaction depicted in Scheme 49 was performed with the non-symmetrical phenyl ethylpropynoate, the only organometallic isomer, analogous to **81**, that could be isolated was the one having the ethyl ester substituent linked to the ruthenium atom. When the reaction was performed with internal alkynes substituted by more electron-releasing groups than an ester unit, a different reaction took place (Scheme 50). The identified product was a ruthenium(0) sandwiched between a η^6-benzene ligand and a η^4-isoquinilinium unit. It is noteworthy that no such organoruthenium(0) derivative could be obtained when the ruthenium was η^6-linked to *para*-cymene, as the resulting compounds were very unstable.



Scheme 49. Formation of stable cycloruthenated rings by insertion of an electron-poor alkyne into Ru–C bonds.



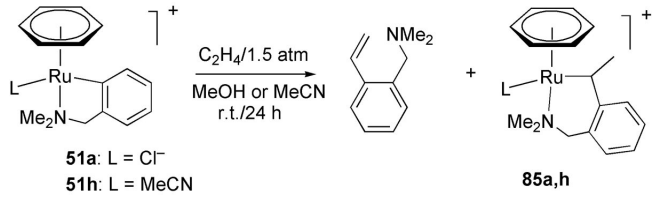
Scheme 50. Formation of isoquinolinium derivatives by reaction of ruthenacycles with electron-rich alkynes.

Ryabov et al. studied the mechanism of the formation of compounds **82**–**84**. They found that the rate-determining step of the reaction was the insertion of the alkyne into the Ru–C bond of the cycloruthenated species.[137] The latter was confirmed by the observation, inter alia, that the electron-donating groups X at the dimethylbenzylamine ruthenacycle favour the insertion, and by the characterization of the inserted products, analogous to **80**. The formation of the isoquinolinium units was thus rationalized as being the result of a reductive elimination between the dimethylamino group and the ruthenated vinyl unit that was formed through insertion of the alkynes into the Ru–C bond of the starting compounds **51**. This C–N bond formation was, however, only possible when the ruthenated carbon atom of the vinyl unit was substituted by an electron-releasing group (Me, Et, Ph). A similar reductive elimination could not be observed for any of the compounds **81a**,**d**–**g**, nor for the compounds obtained with phenyl ethylpropynoate, which bore the ester group at the carbon atom linked to Ru.

Interestingly, the isoquinolinium ligands could be easily decoordinated from the Ru^0 species by using a smooth oxidant such as $CuCl_2$, thus regenerating the starting material, i.e. $[(\eta^6\text{-benzene})RuCl_2]_2$, that was used to synthesize the cycloruthenated compounds.[54] The elementary steps of a catalytic process leading from *N*,*N*-dimethylbenzylamines to the heterocycles by reaction of alkynes with the cycloruthenated species were thus identified. The catalytic activation-functionalization of a C–H unit by ruthenium could thus be achieved in principle. Unfortunately, all attempts made to perform the reaction between dimethylbenzylamines (dmba) and alkynes, by using catalytic amounts of various ruthenium derivatives and the reagents necessary to induce the cyclometallation, failed so far.[139]

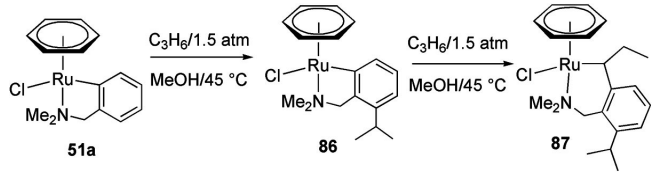
The insertions of alkenes into Ru–C bonds that will be discussed in the next paragraphs are strongly connected to the catalytic insertion of alkenes into the C–H bonds at the *ortho* positions of aryl moieties substituted by directing groups such as ketones or imines reported by Murai et al.[140,141] These results, obtained with catalytic amounts of ruthenium and without isolating the cycloruthenation compounds, are out of the scope of this review article and hence will not be discussed here, as several reviews reporting this important topic have been published recently.[142,143]

The reaction of compounds such as **51a** with ethylene afforded at room temperature a mixture of products as shown in Scheme 51.[144,145]



Scheme 51. Heck-type reaction vs. one-carbon insertion of ethylene into the Ru–C bond.

The yields of the various products were very much dependent upon the nature of the ligand L and of the solvent used. In methanol, compound **85** was the major product of the reaction, whereas in MeCN, the reaction afforded either the *ortho*-vinyl-dmba product with 50% yield with **51a** as starting material or the organometallic product **85h** with 38% yield, the starting product being **51h**. The formation of stoichiometric amounts of the "Heck-type organic product" was rationalized by the formation of an unstable organometallic intermediate in which the ethylene had inserted into the RuC bond of **51**. The β-elimination process then led to *ortho*-vinyl-dmba and a ruthenium hydride species. The hydrometallation of the novel alkene unit should then take place to afford **85**. This latter product slowly rearranged into another cycloruthenated compound in which the other *ortho* position of the aryl ring was metallated, thus allowing a second addition of an alkene at the new Ru–C bond (see Scheme 52 for a related example). The scope of this reaction was unfortunately rather limited, as the only other alkene that was found to be reactive with **51a** was propene. This latter reaction led, however, to a regioselective semicatalytic reaction, as two C_3 alkyl groups were found on the phenyl ring in the final product; the mono-inserted product analogous to **85** was not isolated, most probably because of steric effects at the ruthenium centre.

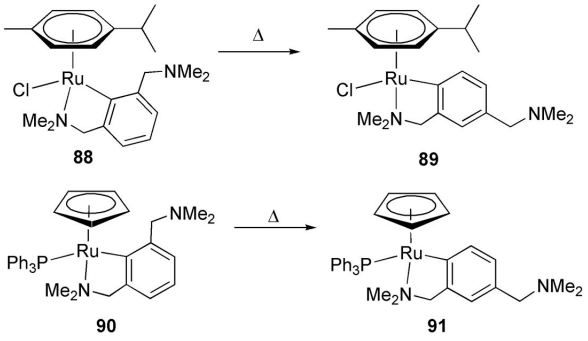


Scheme 52. Stepwise insertion of one and two propene molecules into the Ru–C bond.

The reaction above could not be made catalytic in ruthenium, and this was most probably due to the strength of the N–Ru bond in compounds such as **85** or **87**. As a consequence, the modified cycloruthenated ligand could not be easily removed from the coordination sphere of the metal, hence the organoruthenium species were dead ends.

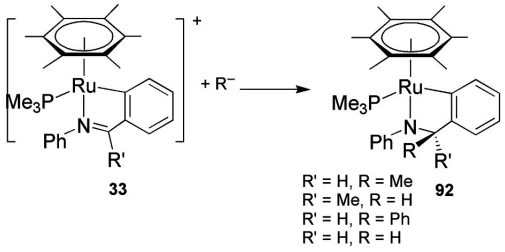
As for the formation of **86**, depending upon the steric effects around the Ru atom, rearrangements of the ruthenacycle may occur to form a less strained metallacyclic unit: van Koten et al.[146] have found that pincer derivatives in

semisandwiched compounds such as **88** and **90**, which were obtained by transmetallation reactions from lithiated pincer ligands, may be readily isomerized to afford **89** and **91**. The isomerizations thus resulted in release of steric tension around ruthenium brought about by the noncoordinated CH_2NMe_2 arm of the pincer in the starting compounds. Mechanistic studies and deuterium-labelling experiments showed that the isomerization took place by decoordination of the nitrogen, which was the rate-limiting step of the reaction, followed by fast successive metallation-demetallation of the methyl substituents of the NMe_2 groups, leading finally to the products by reductive elimination (Scheme 53).



Scheme 53. Isomerization of sterically strained ruthenacycles.

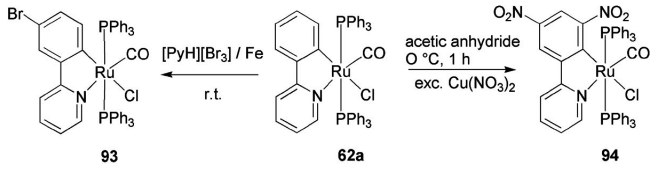
A nice example of the extra stability brought about by the formation of the metallacyclic unit is presented in the following case (Scheme 54). It was found that the C=N unit of **33** reacted with strong nucleophiles such as hydrides or carbanions to afford **92**. Weaker nucleophiles such as alkoxides did not react with this species. This behaviour is in marked contrast to the metallation reaction (see Scheme 20 above), from which all traces of water must be excluded to prevent nucleophilic attack of water on the imine carbon. Here the formation of the metallacyclic ring has significantly decreased the electrophilicity of the imine carbon atom.[53]



Scheme 54. Reaction of a metallacyclic unit with strong nucleophiles.

3.2. Electrophilic Substitution at Cycloruthenated Aryl Groups

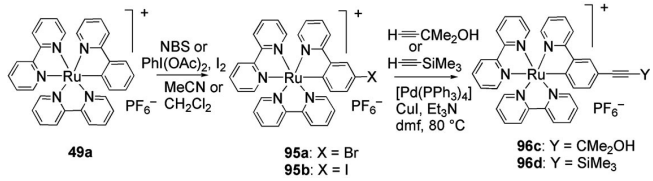
While this review article was in preparation, a related paper by van Koten et al. appeared, which reported some aspects of the reactivity of cyclometallated compounds obtained with platinum group metals.[147] The electrophilic substitution at metallated aryl units is described in detail for several cyclometallated compounds; therefore, this section will only briefly report the main results concerning cycloruthenated compounds. The readers are invited to consult this review for more details about these reactions. Electrophilic substitution at the *para* and *ortho* positions of aryl units substituted by ruthenium was investigated first by Roper et al.[148] These authors found that the aryl–Ru bond was very much resistant towards electrophilic substitution reaction conditions, as the aryl rings σ-bonded to ruthenium could be nitrated in the presence of $Cu(NO_3)_2$ and acetic anhydride without affecting the Ru–C bond. Moreover, the resulting 4-nitrophenyl ligand could be reduced with zinc and HCl to afford a 4-aminoarylruthenium complex that could be acetylated to the corresponding amide, which demonstrates the great robustness of the Ru–C bond.[149] Cycloruthenated phenylpyridine is more prone to be nitrated than free 2-phenylpyridine, as *ortho* and *para* substitutions of the phenyl group were found to take place in presence of an excess of copper nitrate in acetic anhydride, however in low yield (Scheme 55). On the other hand, mononitration takes place at the phenyl group of the nonmetallated ligand with HNO_3 in concentrated H_2SO_4 at 100 °C. Selective bromination at the *para* position of the same cycloruthenated ligand occurred with pyridinium tribromide and catalytic amounts of iron (Scheme 55).



Scheme 55. Electrophilic substitution at the ruthenated phenyl unit of 2-phenylpyridine.

Closely related results were obtained with cycloruthenated ligands such as 2-phenylquinoline or 2,3-diphenylquinoxaline.[112]

On the way to dinuclear mixed-valence complexes as chemical models of molecular wires, Coudret et al. functionalized cycloruthenated phenylpyridine species according to the procedure depicted in Scheme 56.[150]



Scheme 56. Functionalization procedure of cycloruthenated phenylpyridine.

Several dimetallic compounds linked by various spacers were synthesized by using Sonogashira-type reaction conditions. One example is given in Figure 8, other examples include one or two triple bonds or bis(ethynyl)aryl groups with aryl = benzene, thiophene or anthracene.[151]

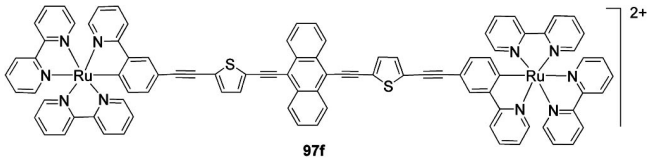
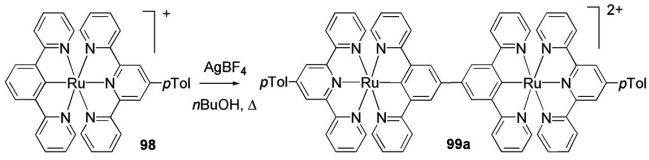


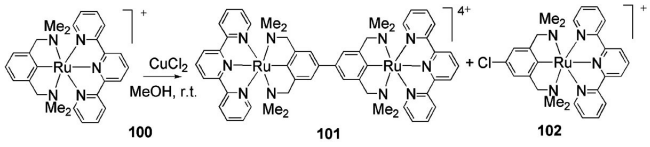
Figure 8. Example of a molecular wire obtained from parafunctionalized cycloruthenated phenylpyridine with alkynyl units.

The *para* position of the cyclometallated phenyl ring of pincer-type ligands was also activated towards C–C coupling in the presence of an excess of oxidants. Sauvage et al. described the first synthesis of dinuclear ruthenium derivatives obtained by the reaction of a monomeric cycloruthenated species with an excess of silver tetrafluoroborate in refluxing butanol (Scheme 57).[152]



Scheme 57. Dimerization of a cycloruthenated species through oxidation by a silver salt.

The Cu^{II}-mediated C–C coupling of a related Ru(pincer) derivative was reported by van Koten et al. (Scheme 58).[153] In contrast to what was observed for the silver-mediated reaction, the latter afforded a dinuclear Ru^{III} species.



Scheme 58. Dimerization of a cycloruthenated pincer species through oxidation by a copper(II) salt.

The mechanism by which the *para* C–H bond was activated in these reactions remains unclear. It is believed that the first step of the reaction involved the oxidation of the ruthenium centre, which in turn resulted in the activation of the *para* position of the aryl group bound to Ru, which, reacting further with copper, would give cluster aggregates. These latter species should then lead to radical organoruthenium(III) species that afford the dinuclear species or the *para*-chloro derivative observed.

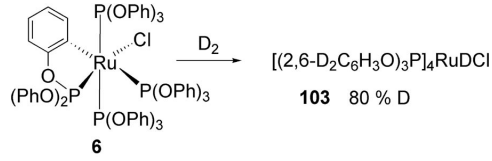
4. Application of Cycloruthenated Compounds as Catalyst Precursors

Although ruthenium complexes have been widely investigated in homogeneous catalysis,[154] their *ortho*-metallated partners are still not thoroughly used and hence they have probably not yet demonstrated their full potential. However, a few examples of cycloruthenated complexes have shown good activities in catalysis and are promising for the future, if one takes into account the high potential of the corresponding cyclopalladated species.

The first applications described hereafter (*ortho*-deuteration, C–C bond formation and hydrogenation) are somehow anecdotic uses of ruthenacyclic compounds, in contrast with the hydrogen-transfer reaction, which overwhelms all other fields of catalytic applications.

4.1. *ortho*-Deuteration of the Ligands

The very first application in organic synthesis of *ortho*-metallated ruthenium complexes was the reaction of *ortho*-deuteration of C–H bonds in phosphane and phosphite ligands. By treating the *ortho*-bonded complex **6** with D_2, the *ortho*- and metal-deuterated complex **103** was obtained with 80% of *ortho*-deuteration (Scheme 59).[20,155] This exchange was explained by the reversible oxidative addition of the *ortho*-phenyl C–H bond to the metal. These authors have also shown that $[(C_6H_5)_3P]_3RuHCl$ was an efficient catalyst for the *ortho*-deuteration of triphenylphosphane as $(2,6\text{-}D_2C_6H_3)_3P$ was obtained in 83% yield, with more than 95% deuterium at the *ortho* positions after 30 h at 100 °C under a flow of D_2.

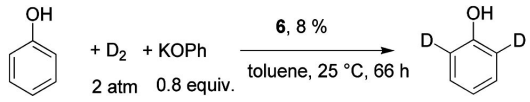


Scheme 59. *ortho*-Deuteration of triphenyl phosphite by cycloruthenation.

Illustration of the reversibility of the C–H activation shown by deuterium exchange has also been reported by Chaudret and Poilblanc. They found that the highly reactive tetrahydride RuH_4L_3 [L = PCy_3, $PiPr_3$, $P(NEt_2)_3$] led to the "RuH_4L_2" species by dissociation of a phosphane; this species catalyzed (at room temperature and in the dark) the spontaneous H–D exchange between the phosphane protons and a deuterated solvent through a series of inter- and intramolecular C–H activation reactions.[26] For the phosphane $PiPr_3$, up to 70% of the protons were exchanged, which represented 44 protons exchanged per ruthenium atom; hence this reaction could be considered as catalytic in ruthenium.

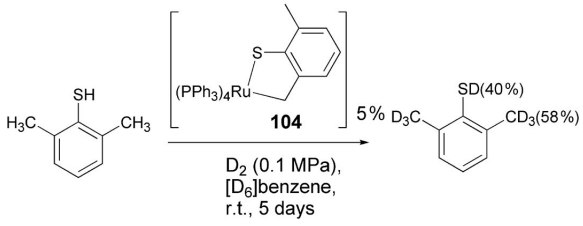
4.2. *ortho*-Deuteration of the Substrate

Lewis and co-workers have taken advantage of the deuteration of the anchored ligand in *ortho*-metallated ruthenium complexes. They have demonstrated that **6** can be used as a selective catalyst for the H–D exchange at the *ortho* position of phenols (Scheme 60), in the presence of KOPh as transesterification cocatalyst, which facilitates the exchange of the deuterated phenoxide at the phosphorus centre in **103**.[156] This reaction was the very first example of catalysis by an *ortho*-metallated complex with use of a coordinating atom (e.g. phosphorus) as a chelating assistance to enhance catalytic activity.



Scheme 60. Ruthenacycle-catalyzed *ortho*-deuteration of phenol.

More recently, in 2005, thioruthenacycle **104** was found to catalyze similar selective and facile sp^3 C–H deuteration reactions of the *ortho*-methyl and -mercapto groups in 2,6-dimethylbenzenethiol under a D_2 atmosphere (Scheme 61).[157] It was demonstrated also in this case that upon exposure of H_2, the Ru–C bond was reversibly hydrogenolyzed, leading to the corresponding (hydrido)(thiolato)-ruthenium complex.

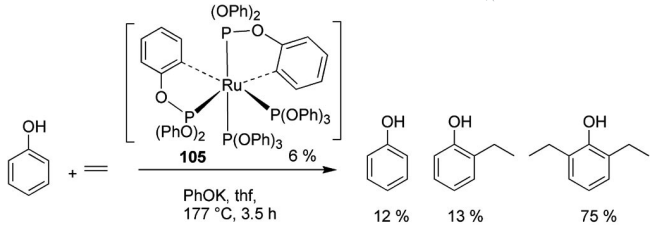


Scheme 61. H–D exchange via a thiocycloruthenated catalyst.

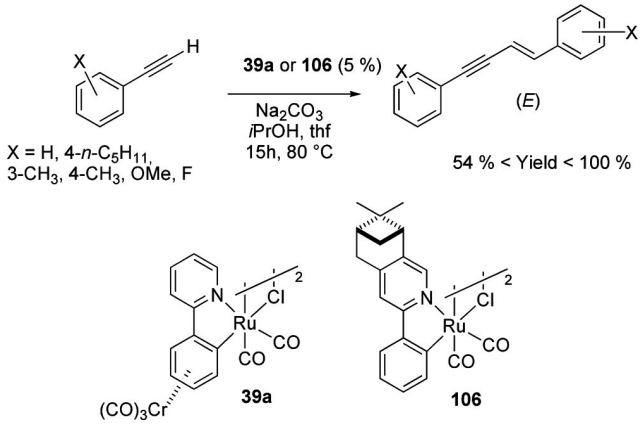
4.3. C–C Bond Formation

One major endeavour in C–H activation is to uncover new routes to selective C–C bond formation. Ruthenacycles were involved as intermediates in a Murai-type coupling reaction between aryl ketones and alkene derivatives (see above). In the early 1980s, Lewis and co-workers had already discovered that ruthenacyclic complexes could lead to alkylation catalysts. The reaction of **6** with ethylene above 120 °C gave a complex mixture of products containing ruthenium complexes with substituted phosphite and the corresponding free phosphates.[23] Using a procedure closely related to the one described in Scheme 62 for the *ortho*-deuteration of phenol, they could achieve the coupling of phenol with ethylene in the presence of the bis-*ortho*-metallated complex **105** leading to the formation of 2,5-diethylphenol in good yield. The key step of this reaction is the exchange of an alkylated phenol bonded to the phosphorus atom by a new phenolate. Hence, the phosphorus acts as a directing group as in a Murai-type reaction. Lewis et al. have extended the scope of this reaction by using styrene as olefin, and they obtained up to a 10% yield of low-weight polystyrene.

The ability of (C,N)-chelates containing the $Ru(CO)_2Cl$ motif to promote C–C coupling reactions, as well as hydrogen-atom transfer, has been demonstrated lately.[158] Both complexes **39a** and **106** catalyze the homocoupling of arylethynes, leading efficiently and selectively to the formation of (*E*)-1,4-diaryl-but-1-en-3-ynes (Scheme 63).



Scheme 62. Alkene insertions into the *ortho* C–H bond of phenol catalyzed by a bisruthenacyclic compound.



Scheme 63. Homocoupling of arylethynes catalyzed by dicarbonylchloridoruthenium metallacycles.

4.4. Hydrogenation

Going on with their studies on *ortho*-metallated phosphite ruthenium complexes, Lewis demonstrated that complex **6** was an active catalyst for olefin hydrogenation while the non-*ortho*-metallated analogue $HClRu[P(OPh)_3]_4$ was inactive.[24] The five-coordinate Ru^{II} complex **107** exhibited an activity similar to $HClRu(PPh_3)_3$ or even higher than Wilkinson's catalyst $ClRh(PPh_3)_3$, although its use in synthesis was limited by its high air sensitivity (Figure 9). Surprisingly, *ortho*-metallated phosphane complex **108** was inactive in the hydrogenation of alkynes.[22]

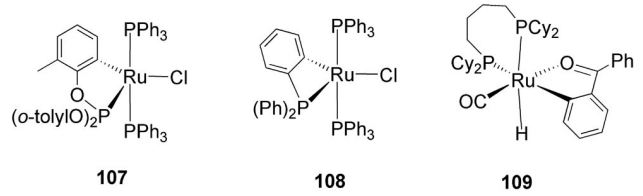


Figure 9. Efficient cycloruthenated hydrogenation catalysts.

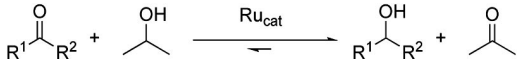
Fogg et al. have found that the isolated *ortho*-metallated intermediate **109** was even more active than the precursor $[RuCl_2(dcypb)(CO)]_2$ [dcypb = 1,4-bis(dicyclohexylphosphanyl)butane] in the hydrogenation of benzophenone.[159]

Reduction by hydrogenation of aliphatic and aromatic nitro compounds and nitriles, aliphatic ketones and Schiff bases to their corresponding saturated products has also been successfully performed with thermally stable dinuclear *ortho*-metallated ruthenium(II) of the type $[RuL(CO)_2Cl]_2$,

[LH = 2-phenylpyridine, benzo[*h*]quinolidine, 1-phenylpyrazole and azobenzene] under high pressure (110 bar) and high temperature (150 °C) in dmso or dmf.[160–162] Saha et al. have also found that the same family of catalysts could promote the reductive N-carbonylation of nitroaromatics under drastic conditions.

4.5. Reduction of Ketones by Transfer Hydrogenation

One area in which ruthenacyclic complexes have found widespread catalytic application is the reduction of carbonyl compounds by hydrogen transfer (HT). This reaction was performed by using 2-propanol as a hydrogen source that reduces the ketone, leading to the corresponding alcohol, as depicted in Scheme 64.



Scheme 64. Reduction of ketones by hydrogen transfer.

Typical experiments have been carried out with model substrates such as cyclohexanone (Table 1), benzophenone (Table 2) and acetophenone (Table 3). However, a larger diversity of ketone substrates have been used (see a selection in Figure 10).

In 2000, van Koten showed that pincer-type arylruthenium(II) complexes containing the monoanionic terdentate bis(amino)aryl (NCN) and the bis(phosphanyl)aryl (PCP) ligands (Figure 11, complexes **23a**,**b**, **25a**) were able to catalyze the reduction of ketones with high activities (Table 1 entries 1–5, Table 2 entries 1–2, TOF up to 33600 h^{-1}) after activation with a base (KOH).[163] Endeavours to improve those promising results involved modifying the electronic properties of the substituents on the arm of the ligand (Figure 10): more electron-rich [P*i*Pr$_2$,[164] PCy$_2$,[31] P(*p*-OMeC$_6$H$_4$)$_2$, complexes **23c**,**h**,**i** and **110**] and electron-poor[165] [P(*p*-CF$_3$C$_6$H$_4$)$_2$, P(C$_6$F$_5$)$_2$, complexes **23d**–**f**] phosphane ligands have been tested. A general feature is that

Table 1. Reduction of cyclohexanone catalyzed by ruthenacycles.

Entry	Catalyst	Conversion % (time)	*T* [°C]	Loading [mol-%]	Base	TOF [h^{-1}]	Ref.
1	**25a**	>98 (3.3 h)	82	0.1	KOH	1100	[163]
2	**23a**	>98 (1.3 h)	82	0.01	KOH	27000	[163]
3	**23b**	>98 (1.8 h)	82	0.01	KOH	10000	[163]
4	**23b**	98 (10 min)	82	0.1	KOH[a]	33600	[165]
5	**23b**	>98 (2.5 h)	25	0.25	KOH	900	[163]
6	**23c**	96 (30 min)	82	0.1	KOH[a]	8000	[165]
7	**23d**	98 (10 min)	82	0.1	KOH[a]	35700	[165]
8	**23e**	98 (780 min)	82	0.1	KOH[a]	41	[165]
9	**23h**	98 (300 min)	82	0.1	KOH[a]	980	[165]
10	**111a**	78 (2 h)	80	0.2	KOH	n.d.	[166]
11	**112**	>99 (1 h)	80	0.3	KOH	297	[167]
12	**113**	99 (5 min)	82	0.05	NaOH	1.0×10^5	[168]
13	**114**	99 (15 min)	82	0.05	NaOH	19000	[169]
14	**115a**	97 (2 min)	82	0.005	NaOH	1.5×10^6	[170]

[a] Pretreatment (60 min).

Table 2. Reduction of benzophenone catalyzed by ruthenacycles.

Entry	Catalyst	Conversion % (time)	*T* [°C]	Loading [mol-%]	Base	TOF [h^{-1}]	Ref.
1	**25a**	90 (90.0 h)	82	0.1	KOH	83	[163]
2	**23a**	>98 (108.0 h)	82	0.1	KOH	100	[163]
3	**23i**	91 (24 h)	82	0.1	KOH/H_2	n.d.	[31]
4	**23i**	92 (40 h)	82	0.1	KOH	n.d.	[31]
5	**110**	88 (96 h)	82	0.1	none	n.d.	[31]
6	**111a**[a]	97 (2 h)	80	0.3	KOH	145	[166]
7	**111b**[a]	>95 (2 h)	82	1	KOH	n.d.	[171]
8	**112**	>99 (1 h)	80	0.3	KOH	297	[167]
9	**114**	95 (5 min)	82	0.05	NaOH	3.6×10^4	[169]
10	**115a**	98 (10 min)	82	0.005	NaOH	5.3×10^5	[170]

[a] Same results obtained with all catalysts of type **111**.

Table 3. Reduction of acetophenone catalyzed by ruthenacycles.

Entry	Catalyst	Conversion % (time)	*ee* [%]	*T* [°C]	Loading [mol-%]	Base	TOF [h^{-1}]	Ref.
1	**25a**	70 (44 h)		82	0.1	KOH	36	[163]
2	**23b**	100 (0.8 h)		82	1	KOH	2300	[181]
3	**23a**	90 (0.5 h)		82	0.1	KOH	9000	[163]
4	**23h**	>95 (5 h)		82	1	KOH	n.d.	[164]
5	**23i**	>98 (n.d.)[a]		82	0.1	*t*BuOK/H_2	2500	[31]
6	**111a**	89 (3 h)		80	0.3	KOH	88	[166]
7	**112**	97 (1 h)		80	0.3	KOH	291	[167]
8	**113**	99 (5 min)		82	0.05	NaOH	1.1×10^5	[168]
9	**114**	98 (5 min)		82	0.05	NaOH	60000	[169]
10	**115a**	98 (5 min)		82	0.005	NaOH	1.1×10^6	[170]
11	**23g**	98 (1 h)	14	82	1	KOH	n.d.	[175]
12	**23j**	40 (17 h)	18	82	1	KOH	n.d	[164]
13	**23k**	40 (15 h)	12	82	1	KOH	n.d.	[164]
14	**115b**	95 (5 min)[b,c]	87	82	0.05	NaOH	6.0×10^5	[170]
15	**116a**	48 (2 h)	10	20	1	*t*BuOK	n.d.	[176]
16	**116b**	97 (1 h)	38	20	1	*t*BuOK	n.d.	[176]
17	**116d**	95 (20 min)	61	20	1	*t*BuOK	n.d.	[176]
18	**116d**	98 (1 h)	46	82	0.01	*t*BuOK	30000	[177]
19	**116c**	95 (2 h)	85	20	1	*t*BuOK	n.d.	[176]
20	**116e**[c]	49 (1 h)	89	20	2	*t*BuOK	n.d.	[176]

[a] Pretreatment (60 min). [b] The substrate was *o*-MeO-acetophenone. [c] In situ synthesis of the catalyst.

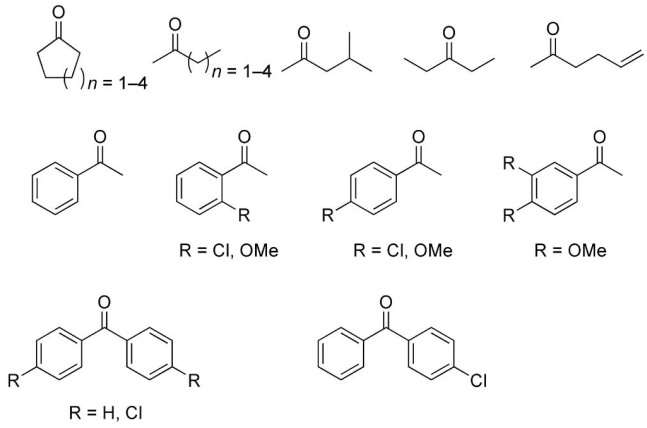


Figure 10. Various ketones reduced by HT.

bis(aryl)phosphane PCP-pincers are more active precatalysts than the electron-rich bis(alkyl)phosphanes (Table 1 entries 2–9, Table 2 entries 2–5, Table 3 entries 3–5). Electron-poor ligands were better precatalysts, except for the very bulky **23e**, which was probably too hindered to be reactive. It must be noted that, for these pincer complexes, a pretreatment with a base was necessary to improve the catalytic activity (Table 1, entries 2 and 3, TOF increased by a factor 3).[31,165]

Not only symmetric pincer-type complexes have been successfully involved in the transfer hydrogenation reaction. Dissymmetric tridentate ONC complexes[166,167,171] (Figure 11, complexes **111**–**112**) presented the advantage of not being air sensitive, so no particular care had to be taken with solvents. However they displayed a lower reactivity in HT compared to other systems.

Superlative activity[172] (TOF over 10^5 h^{-1}) was obtained by assembling in the coordination sphere of the ruthenium both an *ortho*-metallated ligand and a 2-aminomethylpyridine ligand[168,169,173] (complexes **113**–**114**, Table 1 entries 12–13, Table 3 entry 8–9). TOF could be pushed even higher (over 10^6 h^{-1}) by using the terdentate *p*-tolyl-2-aminomethylpyridine (CNN) ligand (complex **115a**, Figure 11), which contained both features (NH_2 moiety and Ru–C bond) and coordinated the metal in a pincer manner.[170,174]

Asymmetric reduction of a prochiral ketone has also been investigated by using chiral catalysts (Figure 11, complexes **25b**, **23g**,**j**,**k**, **115b** and **116a**–**e**; Table 3 entries 11–20). Despite nice strategies (chirality at the benzyl position[175] or chiral phosphorus atom donor[164]) developed by van Koten to achieve asymmetric hydrogen transfer with good *ee* values, good selectivity was not obtained with these complexes (*ee* values below 20%). Better results were obtained with the family of ruthenacycles (**116a**–**e**) derived from chiral benzyl amines with *ee* values ranging from 38% to 89% for the reduction of acetophenone at room temperature.[176,177] In addition, it was demonstrated that catalysts could be used in situ, without time-consuming workup, from commercially available reagents, which is very useful for widespread organic applications (Table 3, entry 20). It is worth noting that those catalysts presented a good reactivity (TOF up to 30000 h^{-1}, Table 3 entry 18) and high enantioselectivity only with a primary or secondary amino ligand: complex **116a** (Figure 11) with a dimethylamino group led to a very low conversion and a low selectivity (Table 3, entry 15). The chiral analogue of **115a** (**115b**, Figure 11) catalyzes the reduction of *p*-methoxyacetophenone with good selectivity (87% *ee*) without any reduction of the rate.[170] These results confirm previous findings[178,179] on the importance of unsubstituted sp^3-nitrogen donors in this reaction, usually called the "NH" effect.[180]

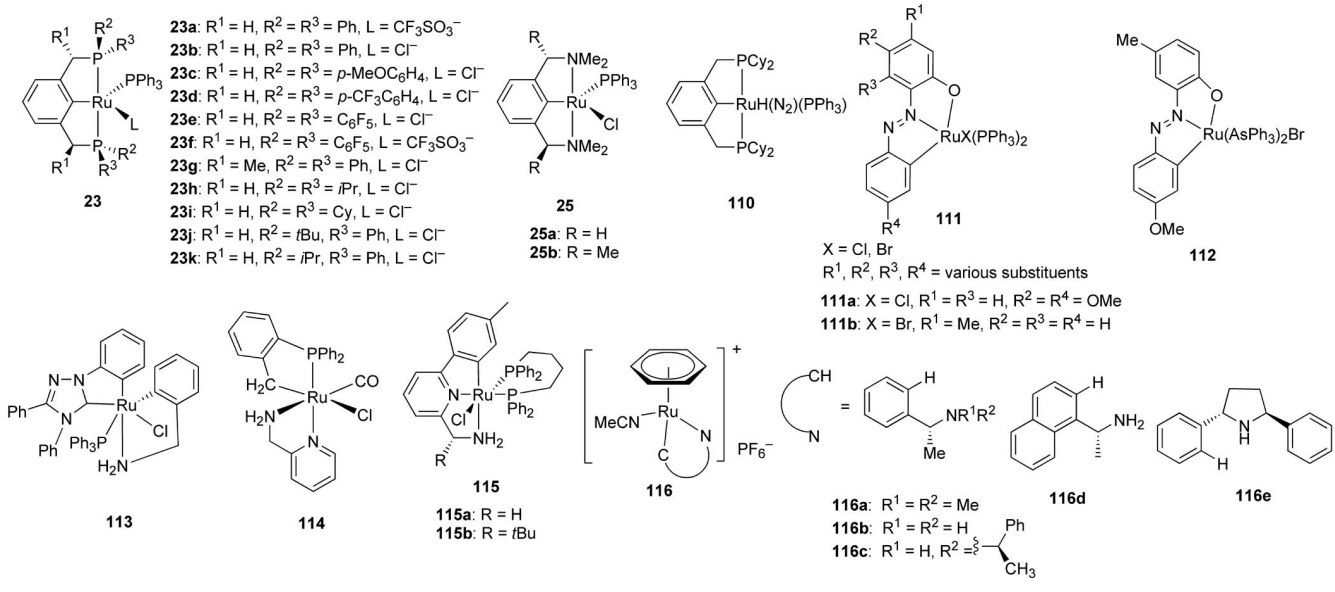


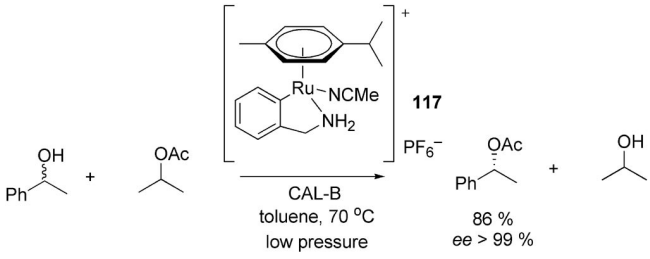
Figure 11. Catalysts of the hydrogen-transfer reaction.

4.6. Reduction of Aldehydes

Catalytic transfer hydrogenation of carbonyl compounds has been extended to the reduction of aldehydes. Aromatic, aliphatic and α,β-unsaturated aldehydes were quickly, quantitatively and chemoselectively reduced to primary alcohols by the terdentate RuCl(CNN)(dppb) catalyst (**115a**, Figure 11) in the presence of potassium carbonate, with TOF values up to 5.0×10^5 h^{-1}.[182]

4.7. Dynamic Kinetic Resolution of Secondary Alcohols

Recently, Arends and co-workers have showed the possibility of using those hydrogen transfer catalysts in dynamic kinetic resolution of secondary alcohols.[64] Catalysts **113**, **115a** and **117** exhibit good-to-excellent racemization rates of (*S*)-phenylethanol in toluene at 70 °C. Ruthenacycle **117** was fully compatible with the enzyme and the acyl residue, leading to the conversion of *rac*-1-phenylethanol into pure (*R*)-1-phenyl ethyl acetate in 86% yield and 99% *ee* after 48 h at 70 °C by using *Candida Antarctica* lipase B as enzyme and isopropyl acetate as acyl donor (Scheme 65).



Scheme 65. Dynamic kinetic resolution of secondary alcohols.

5. Physicochemical Properties

This part of the review encompasses interesting electrochemical and spectroscopic properties (especially photophysical features) of several mono- and polynuclear cycloruthenated complexes. Balzani, von Zelewsky et al. have published a review on the photochemistry and luminescence of cyclometallated complexes in 1992,[183] already including several ruthenium species; many of their conclusions concerning the general physicochemical characteristics of ruthenacycles have been confirmed in subsequent papers.

Indeed, cycloruthenated complexes have many physicochemical properties in common with other coordination compounds with d^6 electronic configuration. However, this class of ruthenium complexes exhibits specific features, which are linked to the ruthenium–carbon bond embedded in a chelate ligand. It is noteworthy that reports on such properties refer to complexes where the carbon atom linked to ruthenium is aromatic, and where the other donor atom of the chelate is mostly an sp^2-hybridized nitrogen. Many authors have cleanly compared the properties of cycloruthenated complexes with closely related homologous noncyclometallated ruthenium complexes. They are essentially the consequence of the anionic nature of the carbon donor atom and its higher ligand field strength compared to other donor atoms such as nitrogen.

Typical mononuclear complexes are shown in Figure 12 and di- and trinuclear complexes are depicted in Figures 13 and 14. Counteranions (PF_6^-, BF_4^-, ClO_4^-, $CF_3SO_3^-$, etc.) are not mentioned for the sake of clarity. The oxidation states of the Ru atoms are those of the isolated complexes; the same compounds could be mentioned throughout chapter 5 with different oxidation states.

The question that is addressed through the study of the polynuclear complexes shown in Figures 13 and 14 is whether the metal centres interact with each other. In this regard, a large variety of ditopic ligands with mostly unsaturated, more or less long spacers have been reported.

5.1. Redox Properties

A host of cycloruthenated complexes has been analyzed at room temperature by cyclic voltammetry. The most widespread solvents used for electrochemical analysis were acetonitrile or dichloromethane, but various other solvents such as methanol, chloroform, dmso, dmf or thf have also been employed. Most publications have used SCE as standard electrochemical reference, and all potentials quoted hereafter are reported vs. SCE.

The Ru^{II}/Ru^{III} Redox Couple

All voltammograms exhibited at least one metal-centred monoelectronic Ru^{II}/Ru^{III} wave, which was/were almost always reversible or quasireversible with few exceptions.[185–187] Those were oxidation or reduction processes depending on the oxidation state of ruthenium in the analyzed complex (mostly +2). The wave assignment could be supported by theoretical calculations.[188] The majority of the reported standard redox potentials, E^0, ranged in the 0.2–1 V bracket, which was considered as rather low. Many authors have compared them with those of noncyclometallated parent complexes (where the carbon donor atom is usually replaced by a nitrogen donor atom) and observed a systematic cathodic shift, by ca. 0.5 to 1 V.[35,185,189–193] For instance, an early report of cathodic shift mentioned a value of 0.66 V for complex **49a**, vs. 1.35 V for the parent complex, $[Ru(bipy)_3]^{2+}$.[194] This electrochemical shift to lower potentials upon cycloruthenation has generally been interpreted as the result of a decrease in the ion charge of the complex and an increase in the electron density on the metal atom caused by the strong σ-donor carbanion, resulting in an elevation of the energy of the t_{2g} orbital. This property led to a useful application of cycloruthenated complexes as electron shuttles (see Section 6.1).

Incidentally, some cycloruthenated complexes had Ru^{II}/Ru^{III} potentials lying outside the usual range. Thus, Yam et al. reported higher values (1.66–1.86 V) for complexes **122a**–**d** that bear an aminocarbene C,C ligand; on the basis of theoretical calculations, they considered that the HOMO

involved in the irreversible oxidation process was not purely metal-centred.[186] Conversely, values in the –0.66 to –0.35 V range were found for ruthenium complexes **50a**–**d**,[102] **111**[166,171,195,196] and **136b**,[197] which are characterized by a high electron density at the metal, either because of anionic ancillary ligands or because of double cyclometallation.

As expected, the presence of electron-withdrawing substituents on the ligand (especially on the ruthenated aro-

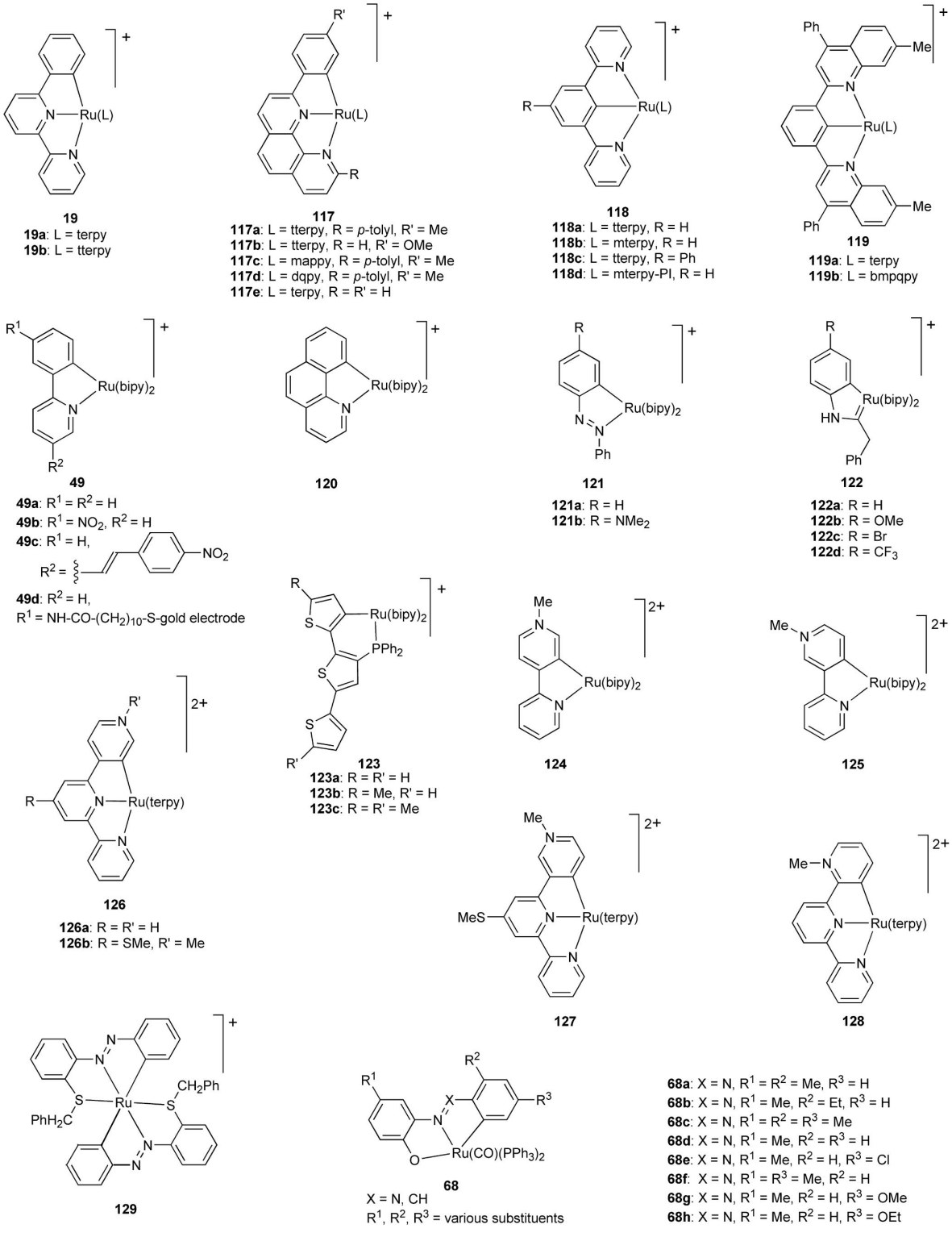


Figure 12. Mononuclear cycloruthenated complexes showing interesting physicochemical properties: bipy = 2,2′-bipyridine; terpy = 2,2′:6′,2′′-terpyridine; mterpy = 4′-methyl-2,2′:6′,2′′-terpyridine; tterpy = 4′-*p*-tolyl-2,2′:6′,2′′-terpyridine; mterpy-PI = 4′-pyromellitimidomethyl-2,2′:6′,2′′-terpyridine (see ref.[184]); mappy = 2-*p*-anisyl-9-(4-methyl-2-pyridyl)-1,10-phenanthroline; dqpy = 2,6-diisoquinolyl-4-*p*-tolylpyridine; bmpqpy = 2,6-bis(7′-methyl-4′-phenyl-2′-quinolyl)pyridine.

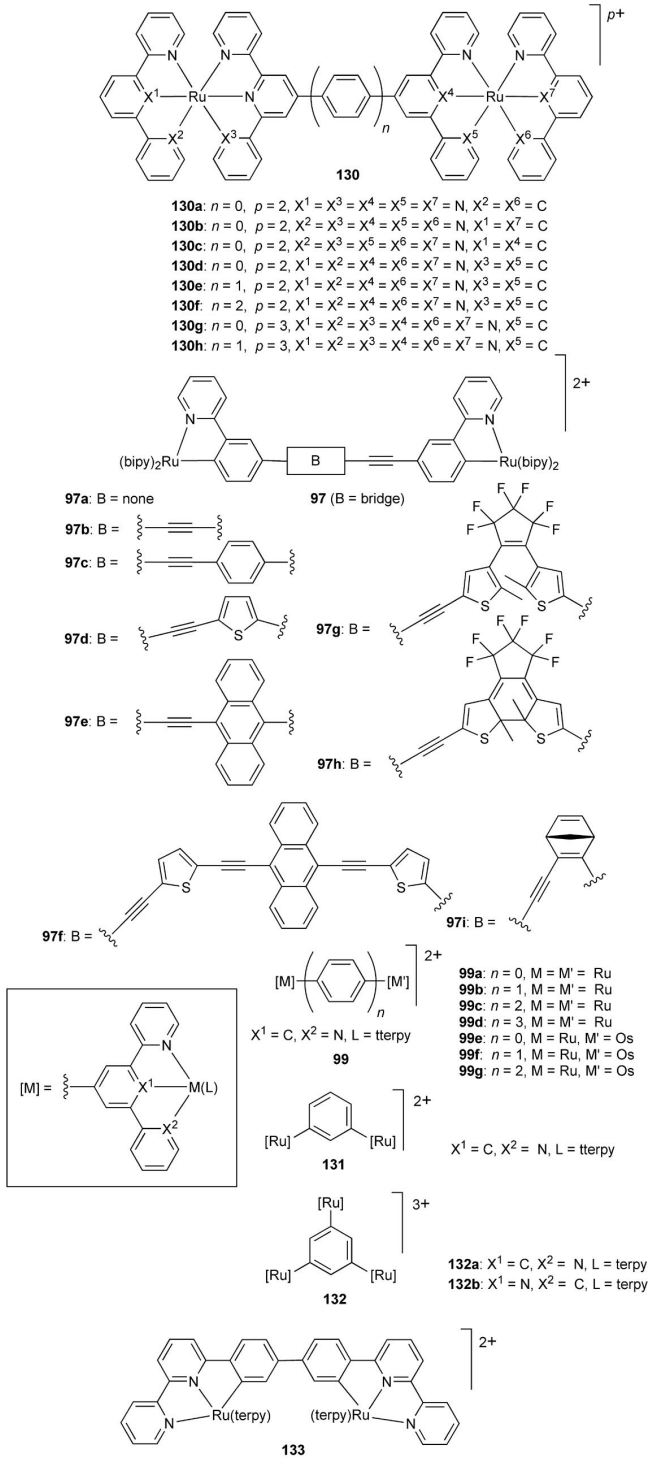


Figure 13. Di- and trinuclear cycloruthenated complexes showing interesting physicochemical properties: terpy = 2,2′:6′,2′′-terpyridine; tterpy = 4′-*p*-tolyl-2,2′:6′,2′′-terpyridine.

matic group) led to an increase in E^0; conversely, electron-donating groups induced a cathodic shift, reflecting a stabilization of the +3 oxidation state.[44,150,193,194,198] Hammett plots of E^0 vs. σ values have been found to be linear for complexes **68** and **111**.[171,196,199] In heterodinuclear cycloruthenated complexes, the presence of another metal complex (Zn porphyrin, Os, Pd) in the molecule led to only little change in E^0.[200–203] Similarly, Hammarström, Johansson et al. observed that Ru^{II}/Ru^{III} potentials for homodinuclear monocycloruthenated complexes were similar to those for each of the monometallic units, suggesting small (if any) electronic coupling between the two metal centres in the ground state.[184,204]

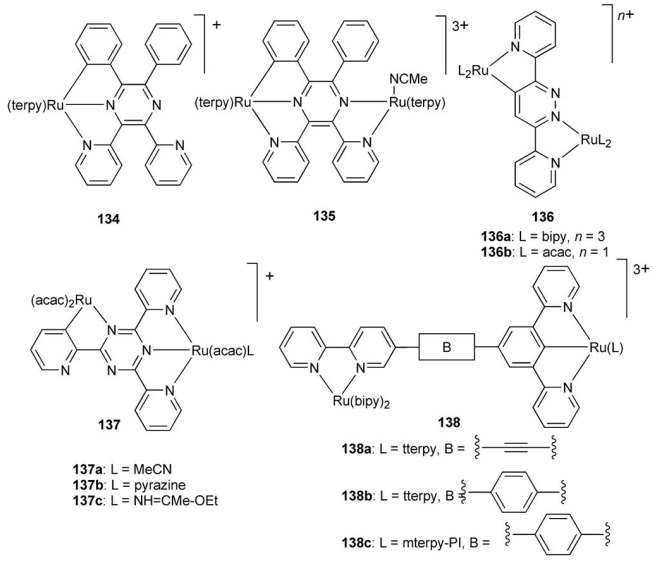


Figure 14. Dinuclear monocycloruthenated complexes showing interesting physicochemical properties: acac = acetylacetonate; bipy = 2,2′-bipyridine; terpy = 2,2′:6′,2′′-terpyridine; tterpy = 4′-*p*-tolyl-2,2′:6′,2′′-terpyridine; mterpy-PI = 4′-pyromellitimidomethyl-2,2′:6′,2′′-terpyridine (see ref.[184]).

The voltammograms of dinuclear complexes with two equivalent cycloruthenated units and various spacers potentially displayed two one-electron Ru^{II}/Ru^{III} waves, corresponding to the $Ru^{II},Ru^{II}/Ru^{II},Ru^{III}$ and $Ru^{II},Ru^{III}/Ru^{III}$, Ru^{III} redox couples. Only one value of E^0 was reported for several of them, viz. **97g–i**, **99b**,**c**, **130d–f** and **133**;[190,198,200,205,209,210] both waves were superimposed in a two-electron wave. Similarly, trinuclear Ru^{II} complexes **132a**[211] and **132b**[209] exhibited a single, reversible, three-electron wave. This was often interpreted as the result of a lack of significant ground-state metal–metal interaction; no interaction at all leads theoretically to a statistical value of 4 for K_c.[190] Various explanations have been proposed to account for this quasi-absence of electronic communication: dihedral twist between aromatic ligand and aromatic spacer, inducing low mixing of orbital systems;[200] components linked through the *meta* position;[211] or long metal–metal distance.[151,190]

With regard to complexes **97a–f**, **99d**, **130b** and **131**, E_1^0 and E_2^0 were too close for the voltammogram to present two distinct anodic waves, but these values could be determined by means of differential pulse voltammetry (Table 4). The corresponding comproportionation constant was then low (4 to 45), which again accounted for poor electronic communication between the two ruthenium centres. It is interesting to note a continuous decrease in K_c correlated with

an increase in the intermetallic distance in the series **97a**–**f**[151] and **99a**–**d**,[190,206] although it cannot be considered as the only parameter involved.[206]

Table 4. Electrochemical data related to the Ru^{II}/Ru^{III} couple for bis-cycloruthenated complexes.[a]

Complex	E_1^0 [V]	E_2^0 [V]	K_c[b]	Ref.
97a	0.453[c]	0.551[c]	45[c]	[151]
97b	0.450[c]	0.579[c]	22[c]	[151]
97c	0.479[c]	0.547[c]	14[c]	[151]
97d	0.485[c]	0.542[c]	9[c]	[151]
97e	0.487[c]	0.544[c]	9[c]	[151]
97f	0.498[c]	0.541[c]	5[c]	[151]
97g	0.53		11[c]	[205]
97h	0.52		12[c]	[205]
97i	0.50		13[c]	[205]
99a	0.340	0.505	690	[190]
99b	0.510		16[d]	[190]
99c	0.515		6[d]	[190]
99d	0.48[c]	0.49[c]	4[c]	[206]
101	0.065	0.24	900	[207]
130a	0.52[c]	0.66[c]	222[c]	[206,208]
130b	0.51[c]	0.578[c]	15[c]	[206]
130c	0.46[c]	0.61[c]	422[c]	[206]
131	0.48[c]	0.54[c]	10[c]	[206]

[a] Standard redox potentials (V vs. SCE) from cyclic voltammetry. [b] Comproportionation constant. [c] Determined from differential pulse voltammetry. [d] Determined from redox titration.

By contrast, the four complexes **99a**, **101**, **130a** and **130c** were distinguished by their well-separated Ru^{II}/Ru^{III} waves and by their high K_c value (222–900) (Table 4), indicating a large degree of electronic coupling between the metal atoms. This is remarkable because both cycloruthenated moieties were structurally equivalent within the complexes. With a roughly equal intermetallic distance (ca. 11 Å), K_c was far superior for **99a** than for a parent noncyclometallated Ru_2 complex;[152] this is obviously an intrinsic property of dimeric ruthenacycles, as far as the Ru···Ru distance was also approximately 11 Å in the three other complexes. This distance was the shortest among those of the complexes reported in Table 4; it is not surprising that a short intermetallic distance is a necessary (but not sufficient) condition for a high K_c value. Incidentally, the redox potentials of **101** were markedly low (the first one was 0.065, which fell out of the classical 0.2–1 V range); this was probably due to the donor effect of the NMe_2 substituents as compared to pyridine groups.

Indeed, the consequence of important values of K_c was a high stability of the Ru^{II},Ru^{III} mixed-valence complexes, which have specific electronic absorption properties (see Section 5.2).[152] However, the observation of a single two-electron Ru^{II}/Ru^{III} wave did not preclude the generation of appreciable amounts of the mixed-valence complex,[190,205,206] even though some attempts to detect it under these conditions were unsuccessful.[200]

Homodinuclear monocyclometallated ruthenium complexes such as **130g**,**h** and **134**–**138** were another category of dinuclear complexes that were electrochemically characterized by two well distinct Ru^{II}/Ru^{III} waves, with ΔE^0 values ranging from 0.48 to 0.79 V.[184,197,204,209,212] It ensued that K_c was naturally much higher (from 10^8 to 10^{14}) than in bis-cycloruthenated complexes (asymmetry effect). In the mixed-valence dimer, the cycloruthenated part was at the +3 oxidation state while the other part (that bears bipy-, terpy- or acac-type ligands) had the value +2.

Ru^{III}/Ru^{IV} and Other Oxidation Waves

Oxidation waves at potentials higher than that of the Ru^{II}/Ru^{III} couple were observed only in a few specific cases.

The first category included complexes **111**, which bear electron-rich anionic ligands.[166,171,195,196] They were characterized by a low Ru^{II}/Ru^{III} potential (vide supra) and exhibited a quasireversible Ru^{III}/Ru^{IV} wave in a relatively low range (0.58–0.96 V). However, the coulometrically generated Ru^{IV} species was reported as unstable at room temperature.[196] Lahiri et al. also reported a Ru^{III}/Ru^{IV} wave on the voltammogram of the acetylacetonato-chelated monocycloruthenated dimers **136b** and **137a**–**c**, but E^0 was higher (1.1–1.6 V) and the oxidation process was irreversible.[197,213]

The second category concerned the more "classical" complexes **68**,[122,188] **121b**,[194] **123a**–**c**[192,214] and **117e**,[38] which were cationic or neutral when Ru was at the +2 oxidation state. The oxidation wave was assigned or tentatively assigned to the oxidation of the carbanionic ligand. Its reversibility depended on the nature of the ligand, and was within the 0.8–1.4 V range. Wolf et al. reported that E^0 for monoelectronic oxidation of a pentathienylphosphane shifted from 0.99 V (free ligand) to 1.77 V upon P,S chelation but was reduced to 0.80 V upon P,C chelation.[192] Within this second category of complexes, the only report of metal-centred oxidation to Ru^{IV} was the article of Launay, Sauvage et al. concerning the bis-cycloruthenated complexes **99b** and **99c**.[190]

Reduction Waves

Cyclic voltammetry analysis of most cycloruthenated complexes indicated one or several reduction waves at negative potential vs. SCE (up to three for mononuclear complexes and four for dinuclear ones). Among them, a majority was related to reversible or quasireversible electrochemical processes, especially the first reduction wave. Sometimes, the determination of standard potentials was hampered by the superposition of unresolved, ill-defined waves. The first (or only) reduction potential usually ranged within –2 and –1 V but could reach higher values (up to –0.4 V) for complexes bearing strongly π-accepting ligands.[199,215]

It was widely assumed that these waves corresponded to ligand-centred monoelectronic reductions, except for reports by Ramesh et al., who assigned them to the Ru^{I}/Ru^{II} redox couple.[166,199] The reduced ligand was seldom the cyclometallated one;[40,191,193,212,216] the reduction process was rather associated with ancillary π-accepting ligands such as bipyridines or terpyridines. It was established for complex **49a** that it was so because the LUMO of the complex was a π* bipy orbital (in agreement with absorption spec-

tra).[183,194] This interpretation, which inferred that the π* orbital of the cyclometallating ligand was too high in energy to be filled, can probably be generalized to the majority of complexes with other ancillary ligands.[186,187]

A cathodic shift of the reduction waves with regard to noncyclometallated homologous complexes was very often observed. This is similar to the shift of the Ru^{II}/Ru^{III} standard potential but less important ($0.2\ V < \Delta E^0 < 0.6\ V$).[186,192,193,201,217] The interpretation was the same, i.e. an increase in electron density onto the metal because of the strongly σ-donating carbanionic atom that would make the ancillary ligand a poorer π-acceptor. Furthermore, Selbin et al. considered that it was more appropriate to contrast the first reduction potential of complexes **49a**,**b**, **120** and **121a**,**b** with the second reduction potential of the closely related $[Ru(diimine)_3]^{2+}$, because they differed by one charge unit, and indeed they observed that E^0 was still lower for the cycloruthenated complexes.[194]

By contrast with other ruthenacycles, Ward et al.[40] and Tanaka et al.[191,216] reported for cycloruthenated complexes **124**, **126b** and **128** a slight anodic shift (or no shift at all) of the first reduction wave relative to noncycloruthenated homologues. This was ascribed to the strong electron-withdrawing property of the metallated quaternized *ortho* or *meta* pyridinium group. However, quaternization of the nitrogen atom at the *para* position to the Ru–C bond (complexes **125** and **127**) led to a more usual cathodic shift, which was interpreted as an effect of the carbene character of the cyclometallating ligand.[191,216]

5.2. Electronic Absorption Spectroscopy

Absorption spectroscopic analysis of solutions (mostly in acetonitrile) of cycloruthenated complexes in the ultraviolet, visible and near-infrared regions of the spectral range has been a widely used tool to characterize them. Strong bands ($\varepsilon = 10^4$–$10^5\ M^{-1}cm^{-1}$) were usually observed in the UV region; those were assigned to ligand-centred ^1LC (n–π* or π–π*) transitions and have generally not been interpreted in detail. Charge-transfer bands were found in the visible region, which were thoroughly studied, sometimes in connection with the previously mentioned electrochemical features and with theoretical calculations. More specifically, intervalence (IT) bands characteristic of some (but not all) mixed-valence Ru^{II},Ru^{III} complexes lay in the NIR region, up to 2500 nm.

Ruthenium(II) Complexes

Like other ruthenium(II) complexes, mononuclear cycloruthenated species presented absorption bands in the 400–700 nm wavelength range with moderately intense molar extinction coefficients ($10^3\ M^{-1}cm^{-1} < \varepsilon < 3\times10^4\ M^{-1}cm^{-1}$). Those were characteristic of spin-allowed metal-to-ligand charge transfer (^1MLCT).[218] As expected, the extinction coefficients of polynuclear complexes were higher (ca. twice for dinuclear complexes and thrice for trinuclear complexes[209]). With mononuclear complexes, the interpretations were rather straightforward, whereas the UV/Vis spectra of dinuclear complexes could present overlapping bands,[184,204] and detailed assignment was sometimes out of reach.[151]

When the complex bore ancillary polypyridine ligands with low-lying π* orbitals such as bipy or terpy, two accurately assigned MLCT bands were often reported.[39,40,183,184,186,191,194,201,204,219,220] The lower-energy one was roughly located in the 500–600 nm region and was associated with the η^2- or η^3-ancillary ligand, whereas the higher-energy one lay in the 350–500 nm region and was rather associated with the carbanionic chelating ligand. This interpretation was supported for complex **126a** by a bathochromic shift of the high-energy MLCT transition upon deprotonation of the cyclometallating ligand.[220] It was also confirmed by theoretical calculations providing information on the HOMOs and LUMOs of complexes **49a**,**b**, **99a**,**e**, **120**, **121a**,**b** and **122a**–**d**:[186,194,201] the HOMO was found to be predominantly metal-centred (t_{2g} orbital) and the LUMO polypyridine-centred (π* orbital), the energy of the empty orbitals of the cyclometallating ligand being higher. One counterexample was reported by Gourdon et al., who attributed the lowest-energy MLCT transition in the UV/Vis spectrum of complexes **134** and **135** to the carbanionic phenazine-based ligand and the highest-energy transition to terpy.[212] Eventually, when only one band in the visible region was assigned, it was considered as a MLCT associated with the polypyridine[38,189,192,198,217,221] or azopyridine[215] noncyclometallating ligand.

By comparison with closely related noncyclometallated ruthenium complexes, the MLCT $Ru(t_{2g})\rightarrow$polypyridine(π*) or $Ru(t_{2g})\rightarrow$azopyridine(π*) band underwent a bathochromic shift with $\Delta\lambda_m$ values ranging from 20 to 100 nm. This redshift was due to a destabilization of the HOMO by the carbanionic ligand through an increase in the crystal field strength.[39,189,219] Exceptions included complexes **125** and **127** reported by Tanaka et al., where the double bond character of Ru–C *para* to a *N*-methylpyridinium group annihilated the cyclometallation redshift effect.[191,221]

This interpretation also explained the cathodic shifts observed in cyclic voltammetry analyses (vide supra) and the bathochromic shifts in emission spectroscopy (vide infra). Wolf et al. quantitatively correlated the electrochemically determined difference between the ruthenium oxidation potential and the first ligand reduction potential for complexes **123a**–**c**, and the spectroscopically determined energy of the MLCT transition.[192] Incidentally, the UV/Vis spectra of these P,C-coordinated complexes exhibited redshifted ligand-centred π→π* transitions and very weak spin-forbidden ^3MLCT transitions beyond 600 nm that were presumably hidden at much lower wavelengths in their P,S-coordinated homologues.

On the basis of DFT calculations, Lacroix et al. interpreted the band centred at $\lambda_m = 546$ nm of complex **49c** as the result of another kind of charge transfer, one in which the rutheniumphenyl fragment is deeply involved in the donat-

ing moiety of the chromophore and the nitrophenyl fragment in the accepting moiety.[222] Comparison with a similar noncycloruthenated complex demonstrated again a high bathochromic shift (92 nm) characteristic of the ruthenacyclic moiety.

When no π-accepting ancillary ligands like bipy or terpy were present in the coordination sphere, absorption bands in the visible region were still considered as MLCT transitions; the LUMO of the complex consisted mainly of antibonding orbitals of a fragment of the cyclometallating ligand, such as phosphane,[44] six-membered zwitterionic iminium-phenolato,[210,223] azo[199] or imine[166,188] functions. However, they may also be interpreted as d–d transitions.[44]

Sometimes the UV/Vis spectra of cycloruthenated dinuclear complexes presented specific features that revealed sizeable interactions between the ruthenium atoms. Enhanced intensities of low-energy bands (ε up to 67000 $M^{-1}cm^{-1}$) were ascribed to a delocalized excited state or a large transition dipole.[151,184,201,204] Dinuclear complexes **130a**,**d**,**g** underwent important bathochromic shifts with regard to the parent mononuclear species **19a** (respectively 85, 50 and 45 nm), but the related dinuclear complexes **130e**,**f**,**h** and **132b** did not because of longer intermetallic distances.[209]

Ruthenium(III) Complexes

Moderately intense absorption bands ($700 < \varepsilon < 7000$ $M^{-1}cm^{-1}$) that lay at relatively high wavelengths ($570\ nm < \lambda_m < 750$ nm) were reported in the UV/Vis spectra of monomeric cyclometallated[35,152,153,166,171,187,195,196,207] or dimeric monocyclometallated[197] ruthenium(III) complexes. These bands were far stronger in the spectra of cyclometallated Ru^{III},Ru^{III} or Ru^{III},Ru^{III},Ru^{III} species, with molar extinction coefficients ranging from 13000 to 117000 $M^{-1}cm^{-1}$;[151,153,211] for instance, the absorption band at 713 nm of complex **99a** at the Ru^{III},Ru^{III} oxidation state was 55 times more intense than the band at 656 nm of the corresponding Ru^{III} monomer **118a**.[152] Furthermore, λ_m could reach a value as high as 850 nm (complex **97g**).[205]

These bands in the visible region have generally been considered as ligand-to-metal pπ→dπ charge-transfer transitions (LMCT).[152,187,195,196] Yet, they could sometimes be assigned to d–d transitions, the LMCT band then being supposed to lie at a higher wavelength (ca. 420 nm).[166,171]

Mixed-Valence Dinuclear Ru^{II},Ru^{III} Complexes

Stable isolated mixed-valence cycloruthenated species have not often been reported, although compounds **137a**–**c** were indeed isolated Ru^{II},Ru^{III} complexes.[213] Otherwise, they were generated in situ either by controlled potential electrolysis[151,190,197,206] (see Section 5.1), by reaction of a Ru^{II},Ru^{II} complex with a controlled amount of oxidant (e.g. redox titration with Br_2) or by mixing equimolar amounts of Ru^{II},Ru^{II} and Ru^{III},Ru^{III} complexes.[207] They were easier to study than their noncyclometallated counterparts because of the moderate values of the Ru^{II},Ru^{II}/Ru^{II},Ru^{III} couple.[224]

Like their homovalent Ru^{II},Ru^{II} and Ru^{III},Ru^{III} counterparts, charge-transfer bands of Ru^{II},Ru^{III} complexes have been observed in the visible region (up to 900 nm). Some of them were assigned to MLCT transitions associated with the Ru^{II} moiety,[197,225] whereas others (usually lower-energy bands) were assigned to LMCT transitions within the Ru^{III} moiety.[151,184,197] The spectra of complexes **137a**–**c** displayed both kinds of transitions, i.e. MLCT at ca. 550 nm and LMCT at ca. 620 nm.[213]

One striking characteristic feature of polynuclear mixed-valence cycloruthenated complexes was the intervalence charge transfer (denominated IT or IVCT) transition located in the NIR region of the absorbance spectrum. This band provided valuable information about metal–metal communication within the dimeric complex; indeed, it was considered as a probe of electron transfer processes within molecular wires.[151] However, such IT bands were sometimes sought for by in situ controlled oxidation of polycyclometallated Ru^{II} complexes but not detected because of poor ground-state interaction between metal centres.[151,200,205,211] Similarly, although heterodinuclear complexes with a cyclometallated Ru^{III} moiety and a noncyclometallated Ru^{II} moiety should be stable because of their high K_c values (see Section 5.1), the IT bands of the mixed-valence complexes **135**, **137a**–**c** or **138c** were nonexistent or too weak to be detected.[184,212,213]

Absorption data pertaining to intervalence bands of several cycloruthenated complexes are gathered in Table 5. Deconvolution was sometimes necessary to determine cleanly their parameters.[151,190,205] Long-distance intervalence electron transfer within bis-cycloruthenated complexes (among other dinuclear complexes) has been reviewed by Launay,[224] and his principal conclusions are recapitulated

Table 5. Intervalence transfer data of mixed-valence homodinuclear mono- and bis-cycloruthenated complexes.

Starting complex	λ_m [nm]	ε_m [$M^{-1}cm^{-1}$]	$\Delta\tilde{\nu}_{1/2}$ [cm^{-1}]	V_{ab} [eV][a]	Ref.
97a	1800	5790	4680	0.070	[151]
97b	1500	2490	5170	0.045	[151]
97c	1200	2350	3630	0.033	[151]
97d	1300	2430	3920	0.034	[151]
97e	1430	6840	4150	0.055	[151]
97h	1351	1400	5000	0.025	[205]
97i	1818	3460	5000	0.068	[205]
99a	1936	22000	2660	0.127	[190]
99b	1650	6600	5112	0.074	[190]
99c	1214	2200	5714	0.041	[190]
99d	985	924	7500	0.028	[206]
101	1875	33000		0.165[b]	[153]
130a	1657	25000–30000			[208]
	2468	5036	5709	0.078	[206]
130b	1585	1227	5146	0.046	[206]
130c	2360	3648	5374	0.066	[206]
131	1848	270	6503	0.018	[206]
136a	1335	2830	2660		[197]
136b	1295	1800	2790		[197]

[a] Hush formula: $V_{ab} = \{[2.05 \times 10^{-2}(\varepsilon\tilde{\nu}_m\Delta\tilde{\nu}_{1/2})^{1/2}]/R_{MM}\}$ where R_{MM} is the metal–metal distance (from ref.[206]). [b] Calculated in ref.[224]

hereafter. In the case of dissymmetrical monocycloruthenated complexes **136a** and **136b**, the IT band was interpreted as a localized transition from the noncyclometallated Ru^{II} fragment to the cyclometallated Ru^{III} fragment.[197]

The electronic factor, V_{ab}, calculated following Hush's theory reflects metal–metal coupling in localized (class II) mixed-valence systems; it allows to assess the efficiency of the bridging ligand at mediating electron transfer between the Ru sites.[205] In this regard, it is not surprising that V_{ab} roughly followed the same trend as the comproportionation constant K_c calculated from electrochemical data (vide supra).[206] Its value generally ranged from 0.02 to 0.08 eV, but higher couplings were calculated for complexes **99a** (0.127 eV) and especially **101** (0.165 eV). As for K_c, the general trend was a decrease in V_{ab} and λ_m when the metal–metal distance increased. Furthermore, an exponential decrease in V_{ab} vs. R_{MM} was reported for complexes **97a**–**d** or **99a**–**d**; the decay slope was found to be larger than that for noncyclometallated homologues. Bandwidths at half-maximum $\Delta\tilde{\nu}_{1/2}$ were usually of the order of magnitude predicted by Hush's theory; yet narrow IT bands could be interpreted as the result of strong electronic coupling, introducing some class III (delocalized) character.[151,206]

The striking property of bis-cycloruthenated complexes with regard to noncyclometallated parent ruthenium complexes [such as bis(terpyridine) complexes] is a far stronger electronic coupling for a given value of R_{MM}. As a consequence, some of them displayed a significant coupling between metals even with very long interatomic distances (up to 24 Å for complex **99d**). Among the bis-cycloruthenated complexes **99a**–**c** and **130a** with similar R_{MM} values, the largest metal–metal interaction was found in **99a**, in which the carbon atom connected to Ru was located on the bridging ligand and on the metal–metal C_2 axis of the molecule.[206] In addition, Barigelletti et al. found for complex **99a** that 23% of the electronic charge was redistributed in the ground state from the Ru^{II} to the Ru^{III} centre, which is consistent with a high degree of covalency for the Ru–C bonds.[201] Intervalence studies of the related complexes **130d**–**h** would have been warranted for comparison but were not reported. Another complex distinguished by its high V_{ab} value is **97e**, where an anthracene group raises the HOMO of the bridge and enhances the coupling.[151]

Prior to theoretical calculations, it was considered by Collin et al. that the raising of the Ru dπ orbital level by the strong σ-donating cyclometallating ligand was a straightforward explanation for this outstandingly positive effect of cycloruthenation, as it was also for the bathochromic shifts mentioned above.[152] It ensured a better energy matching between the metal orbitals and the LUMO of the cyclometallating ligand. Molecular orbital calculations were carried out in order to assess this effect. Extended Hückel calculations or ZINDO methods (which sometimes fitted better with experimental data) were used.[151,206,224] In the context of the "tight binding model", it was stated by Launay that the main difference between cyclometallated and noncyclometallated complexes "depends on the tail of the wave functions with mainly metal character, (which) in the case of cyclometallated compounds (…) have greater extension on the carbon atom located *para* to the ruthenium–carbon bond, thus ensuring better communication with the bridge".[224] The consequence of the replacement of N by an isoelectronic C^- is a better orbital mixing, i.e. an increased interaction between the ruthenium orbitals and the filled orbitals of the ligand.[206]

Eventually, the presence or absence of an intervalence band depending on electronic communication between the metal atoms has spawned interesting applications in the field of "on/off" (complex **97h** vs. **97g**) molecular switches at a fundamental level.[205]

5.3. Photophysical Properties of Ru^{II} Complexes: Emission Spectroscopy and Other Photoinduced Processes

Some of the cycloruthenated complexes listed in Figures 12, 13 and 14 with ruthenium at the +2 oxidation state were photoluminescent at low temperature (77 K) and/or at room temperature, upon excitation at a wavelength generally corresponding to a MLCT absorption maximum. Quantitative data (sometimes partial) which have been reported when the emission was strong enough are listed in Table 6. Some of these data had been previously gathered and discussed in early reviews.[183,218] These luminescence properties are interesting, because such molecules may find applications as chemosensors, solar cells, flat panel displays or optics, among others.[226]

The complexes mentioned in Table 6 emit at wavelengths within the 680–840 nm range, except complexes of the **68** series, whose emission bands were observed at 450–480 nm. With regard to luminescent noncyclometallated parent ruthenium complexes (when they existed), cycloruthenated complexes underwent a strong bathochromic shift (ca. 100–200 nm), the magnitude of which was comparable to the shift observed in absorbance spectroscopy[183] (vide supra). Emission analysis of aminocarbene complexes **122a**–**d** showed that λ_m increased when the Hammett parameter σ of the substituent borne by the ligand decreased.[186]

No general trend seemed to emerge when comparing the intensity of the emission band of cycloruthenated complexes with that of parent noncyclometallated species. Some in the first category were indeed not or very weakly luminescent;[39,194,221] at room temperature, the quantum yield of complex **19b** was lower than that of $[Ru(tterpy)_2]^{2+}$ ($\Phi_{em} = 3.2 \times 10^{-5}$),[228] whereas complexes **49b**, **117b** and **119b** were not luminescent at that temperature. By contrast, complexes **99a**, **117a**,**c**,**d** and **118a** had a comparable or higher Φ_{em} value than $[Ru(tterpy)_2]^{2+}$, and the luminescence of complexes **68** and **122a**–**d** was reported as intense.[199,226] The quantum yield at 77 K of the homodinuclear complex **136a** was high (0.14), but it was not mentioned whether the luminescence should be assigned to the cyclometallated or the noncyclometallated unit of the complex.[197] It is also worth noting that the (P,C)-chelated complexes **123a**–**c** were

luminescent whereas their (P,S)-chelated homologues were not,[192] which underlines the interest of cycloruthenated compounds in the field of emission spectroscopy. Regarding the excited-state lifetime, τ, the comparison between cycloruthenated and noncycloruthenated was in favour of the second at 77 K. Conversely, at 298 K, the value of τ was only 0.95 ns for $[Ru(tterpy)_2]^{2+}$,[228] whereas superior figures (by up to a factor 100) were reached with cycloruthenated species (Table 6).

It is widely accepted that the luminescence of cyclometallated ruthenium complexes originates from a triplet excited-state ^{3}MLCT.[183,185,226] Selbin et al. stated for complex **49b** that this ^{3}MLCT state contains a significant amount of singlet character due to spin–orbit coupling.[219] This assumption about the nature of the excited state was supported by the absence of photodissociation of the complex resulting from the population of a high-energy metal-centred dd (^{3}MC) state (also referred to as LF). The MLCT excited state is often localized on the noncyclometallating ancillary ligand (e.g. bipy or terpy), although the study of complexes **99a** and **118a** led Barigelletti et al. to conclude that a simple localized description of this state did not provide a clear-cut indication concerning the type of ligand involved, because of the high degree of covalency of the metal–ligand interaction.[201]

The bathochromic shifts are caused by a stabilization of the ^{3}MLCT level resulting from σ–donation by the cyclometallated ligand (Figure 15).[201] Another consequence of cyclometallation is an elevation of the ^{3}MC energy level, a carbon-donor ligand lying high in the spectrochemical series, as previously mentioned (Sections 5.1. and 5.2.).[218] As long as the distorted ^{3}MC state is prone to promote fast, unwanted radiationless deactivation processes, its destabilization favours luminescence with lifetimes of the ^{3}MLCT state in the range 4–106 ns. However, a drawback of the decrease in the ^{3}MLCT energy level is an increase in the nonradiative decay rate according to the energy gap law; this explains why complex **19b** was relatively weakly luminescent.[189] To sum up, the emission intensity is the result of a delicate balance between energy levels of triplet excited states.

Sauvage, Barigelletti, Collin et al. endeavoured to synthesize cycloruthenated complexes that would display long-lived MLCT excited states at room temperature by introducing structural changes in the cyclometallating ligand.[217,227] Indeed, markedly high τ and Φ_{em} values (70–106 ns and 2×10^{-4}–2×10^{-2}, respectively) were reached by complexes **117a**,**c**,**d** stemming from cycloruthenation of 2,9-bis(*p*-tolyl)-1,10-phenanthroline. In this case, the positive effect of cycloruthenation was enhanced by steric protection of the metal and strong rigidifying of the molecular edifice by interligand π–π interaction. Similarly, complexes **119a**,**b** have been designed with extended aromatic frameworks, so that the energy gap between ^{3}MLCT and ^{3}MC levels would

Table 6. Emission spectroscopy data.

Complex	T = 77 K				Room temperature[a]				Ref.
	Solvent	λ_m [nm]	τ [ns]	Φ_{em}	Solvent	λ_m [nm]	τ [ns]	Φ_{em}	
19b	EtCN/*n*PrCN[b]	792	900	2×10^{-4}	MeCN	808	60	5×10^{-6}	[189]
49b	EtOH/MeOH[c]	682	878	3.8×10^{-2}					[219]
68d					CH_2Cl_2	454			[199]
68e					CH_2Cl_2	484			[199]
68f					CH_2Cl_2	480			[199]
68g					CH_2Cl_2	468			[199]
68h					CH_2Cl_2	464			[199]
99a	*n*PrCN	762	440		*n*PrCN	798	3.96	3.7×10^{-5}	[201]
99e[d]	*n*PrCN	ca. 750	0.72		*n*PrCN	ca. 816	0.35	5.4×10^{-6}	[201,202]
99f[d]	*n*PrCN	750	42		*n*PrCN	800	3.5		[202]
99g[d]	*n*PrCN	750	178		*n*PrCN	792	4.9		[202]
117a	*n*PrCN	778	2600		MeCN[e]	802	95	2×10^{-2}	[217,227]
117b	*n*PrCN	704	3600		MeCN[e]	[f]			[217,227]
117c	*n*PrCN	814	2300		MeCN[e]	816	106	1.9×10^{-3}	[217]
117d	*n*PrCN	750	3400		MeCN[e]	778	70.5	2.8×10^{-4}	[217]
118a	*n*PrCN	752	496	7.2×10^{-4}	*n*PrCN	784	4.5	4.5×10^{-5}	[202]
118b					MeCN		4.0		[184]
118c	MeCN	753			MeCN		4.7		[204]
119a	*n*PrCN	735[d]	[f]		MeCN	830			[185]
119b	*n*PrCN	810[d]	2800		MeCN	[f]			[185]
122a	EtOH/MeOH[c]	742			MeCN	808	<100		[186]
122b	EtOH/MeOH[c]	745			MeCN	813	<100		[186]
122c	EtOH/MeOH[c]	706			MeCN	792	<100		[186]
122d	EtOH/MeOH[c]	700			MeCN	782	<100		[186]
123a					MeCN	754[e]	22	ca. 10^{-3}	[192]
123b					MeCN	763[e]		ca. 10^{-3}	[192]
123c					MeCN	772[e]		ca. 10^{-3}	[192]
126a					MeCN	790			[220]
136a	EtOH/MeOH[c]	664		0.14					[197]

[a] T = 298 K, unless otherwise stated. [b] Propanonitrile/butyronitrile (4:5 v/v) glass. [c] Ethanol/methanol (4:1 v/v) glass. [d] Data for the ruthenium-based chromophore. [e] T = 293 K. [f] Not detectable or measurable.

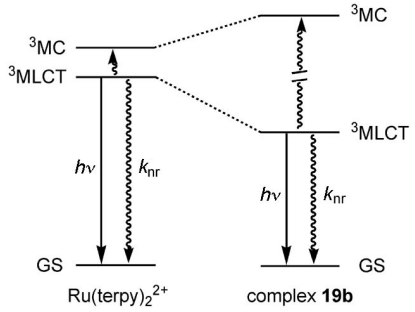


Figure 15. Qualitative energy-level diagram for $Ru(terpy)_2^{2+}$ and **19b** (from ref.[189]).

be increased and luminescence would be enhanced.[185] However, **119b** was not luminescent at room temperature because of excessive internal steric hindrance.

The nature of the excited state of phosphorescent cycloruthenated derivatives of benzo[*h*]quinoline (ligand-localized $^3\pi\pi^*$ including some $^3d\pi^*$ character) has been thoroughly studied at low temperature.[229] In addition, as an application of luminescence, complex **118a** has been grafted to a cyclodextrin in order to design a photoactive receptor unit, and indeed this molecule provided luminescence at ca. 790 nm like **118a** itself.[230]

Several research teams took advantage of the emission properties of cycloruthenated complexes to study intramolecular energy transfer in the heterodinuclear Ru,Os bis-cyclometallated complexes **99e**–**g** (Sauvage, Barigelletti et al.),[201,202] or in the homodinuclear Ru_2 monocyclometallated complexes **138a**–**c** (Hammarström, Johansson et al.).[184,204] In both cases, the energy transfer was found to take place through an exchange-type (Dexter) mechanism.

Indeed, it was stated that the use of a bis-cyclometallating ligand was very conducive to ruthenium-to-osmium energy transfer, allowing it to occur even when the metal–metal distance reached 20 Å.[231,232] The energy transfer took place under a nearly activationless regime and was governed by electronic factors. In comparison with Ru,Os complexes comprising nitrogen-based noncyclometallating ligands, the transfer rate in complexes **99e**–**g** was found to be lower (e.g. $k < 2.2 \times 10^7$–2.6×10^9 s^{-1} vs. $k > 10^{10}$ s^{-1} at 293 K); this was due to the spatial localization of the MLCT excited states involved in the excitation-transfer process (peripheral in the cyclometallated complexes and bridging in the noncyclometallated ones). By contrast with Ru,Os complexes, a bis-cyclometallated Ru,Pd dinuclear complex presented no energy or electron transfer from ruthenium to palladium.[203]

In complexes **138a**–**c**, the energy was efficiently transferred from the RuN_6 unit to the RuN_5C unit with rates ranging from 4.7×10^{11} s^{-1} to 1.4×10^{12} s^{-1}. In addition, complexes **118d** and **138c**, in which a pyromellitimide electron-acceptor group was grafted to terpy, underwent electron transfer from the cycloruthenated unit to pyromellitimide upon photoexcitation of RuN_5C, leading to transient charge-separated states.[184,204]

5.4. Other Analyses

Mononuclear cyclometallated ruthenium(III) d^5 complexes, such as **111** and the oxidized form of **129**, have been analyzed by magnetic susceptibility measurements and/or by electronic paramagnetic resonance.[166,171,195,233] Overall magnetic susceptibility (1.8–2.0 μ_B) data revealed one-electron paramagnetic species. This indicated that the complexes were low-spin ($S = 1/2$) with t_{2g}^5 configuration. EPR spectra recorded at 77 K were rhombic with three different values of *g*, except for the spectrum of the oxidized form of **129**, which was axial (two different values, $g_\perp$ and $g_\parallel$)[233] These EPR results were compatible with a low-spin d^5 configuration, in agreement with the magnetic susceptibility results. The rhombic nature of the spectra reflects severe distortions from an ideal octahedral geometry. However, it does not seem that these EPR features were markedly characteristic of cyclometallating ligands with regard to other κ^3-chelates.

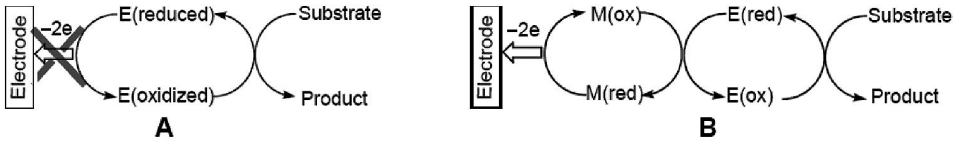
The dinuclear Ru^{III},Ru^{III} complexes issued from **99a**[152] and **136b**[197] were diamagnetic and therefore EPR-silent. For complex **136b**, this was interpreted as the result of a large antiferromagnetic spin–spin coupling of the Ru^{III} centres ($J = -11.5$ cm^{-1}), which had been revealed by the magnetic susceptibility vs. temperature curve. Similarly, Ru^{III},Ru^{III} complex **101** was diamagnetic as shown by its NMR spectrum;[207] thus it could be represented by a Ru^{II}, Ru^{IV} conjugated polyene mesomeric form involving ruthenium–carbon double bonds. By contrast, rhombic signals were found in the EPR spectra of the mixed-valence Ru^{II}, Ru^{III} complexes **136a**,**b**[197] and **137a**–**c**[213] recorded at 4 K and 77 K, respectively. The high *g* anisotropy of **136a** and **136b** suggested strong ruthenium(III)–carbanion interaction.

Lacroix et al. considered that the solvatochromic shift of Ru^{II} complex **49c** suggested important charge-transfer properties, which was promising in the field of nonlinear optics (NLO).[222] Indeed, the NLO response of **49c** was far more important than that of its noncycloruthenated counterpart, with an intrinsic hyperpolarizability equal to 230×10^{-30} $cm^5 esu^{-1}$ (compared to less than 40×10^{-30} $cm^5 esu^{-1}$). In the field of molecular electronics, the synthesis of Ru^{II} complex **49d** embedded in a self-assembled monolayer and fixed at a gold electrode has been reported by Coudret, Bonvoisin et al.; its analysis by impedance spectroscopy revealed very fast electron-transfer kinetics.[234]

6. Miscellaneous Applications

6.1. Cycloruthenated Compounds as Electron Shuttles

Oxidoreductases are enzymes that catalyze oxidative and reductive reactions. Their action on a given substrate requires that electrons be either removed from the reduced state or brought to the oxidized state of the enzymes. Several organic or inorganic molecules are capable of rapidly



Scheme 66. Schematic presentation of direct (nonmediated) electron transfer (**A**) and mediated electron transfer (**B**) from enzyme to electrode (reproduced from ref.[235] with permission).

moving electrons between reduced or oxidized enzyme active sites and transferring them at an electrode. These compounds are referred to as electron shuttles or mediators and many of them are transition-metal-based complexes. A good mediator needs (i) to be sufficiently small to be able to reach usually buried enzyme active sites, (ii) to have a proper redox potential and a medium-independent Nernstian electrode behaviour, and (iii) to have a high electron-exchange rate between oxidized or reduced enzyme active sites.[235]

The functioning of bioanalytical amperometric instruments (biosensors) is based on the mediated electron transfer (MET). The electrons acquired by the enzyme while oxidizing a substrate, as shown in Scheme 66, cannot be readily transferred at an anode. Electron shuttles are therefore needed to transfer these electrons to the electrode, which is then able to "diagnose" the enzymatic redox reaction and "report" adequately on a substrate concentration in a sample.

Tris(diimine) complexes of ruthenium(II) such as $[Ru(N,N)_3]^{2+}$ [(N,N) = 2,2′-bipyridine or 1,10-phenanthroline, see Figure 16] could be ideal mediators for several oxidoreductase enzymes, because of their inertness to substitution and almost diffusion-controlled self-exchange rates providing high reactivity with glucose oxidase. However, the $M^{II/III}$ redox potentials of these dicationic complexes in water are too high, thus excluding their applications in MET-based biosensors. However, the simple replacement of a metal–nitrogen bond by a metal–carbon bond decreases profoundly the redox potentials of such compounds as a result of a combination of two effects, lowering of the overall complex charge and introduction of a strong σ-donor ligand (see Section 5.1). Several cycloruthenated mediators involving 2-phenylpyridine, 2(4-tolyl)pyridine, *N*,*N*-dimethylbenzylamines or 2-phenylimidazole have been synthesized according to Scheme 21. Treating the thus formed cyclometallated compounds with 2,2′-bipyridine and 1,10-phenanthroline (see Scheme 22) afforded a series of target compounds.

The cyclometallated Ru^{III} species generated electrochemically are very reactive in the oxidation of reduced flavin adenine dinucleotide of glucose oxidase. The excellent coupling between this enzyme reduced by D-glucose and the Ru^{III} species is illustrated by the rate constant for complex **141b**, which equals 1.8×10^{-7} M^{-1} s^{-1} at pH 6.7 and 25 °C. Other cycloruthenated complexes are very reactive as well (Table 7). Variation of the nature of cycloruthenated and diimine ligands allows lowering the redox potentials of the complexes practically without compromising the reactivity.

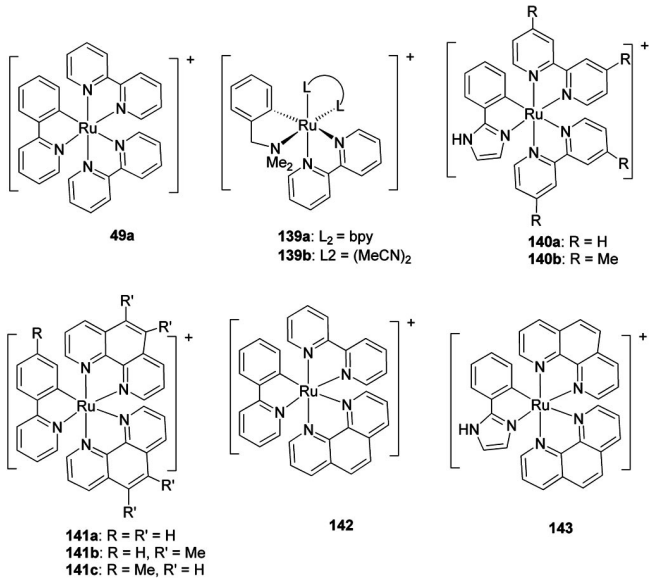


Figure 16. Cycloruthenated complexes used as electron shuttles (see Table 7).

The Δ and Λ enantioisomers of both **49a** and **141a** have been isolated. The rate constant for electron transfer from reduced glucose oxidase (GO from *Aspergillus niger*) have been measured; the electron transfer showed enantioselectivity.[236]

Table 7. Redox potentials of cyclometallated Ru^{II} complexes and rate constants for the electron exchange between Ru^{II}/Ru^{III} species and HRP/GO, taken in part from ref.[235] with permission.

Complex	Redox potentials [mV] (vs. SCE)	HRP: $10^{-8} \times k_7$ [M^{-1} s^{-1}]	GO: $10^{-7} \times k_{12}$ [M^{-1} s^{-1}]	Ref.
49a	280 [a]	0.3	0.35	[61]
139a	190 [a]	0.30	1	[61]
139b	300.[b]	n.r.[c]	0.20	[237]
140a	205 [a]	0.23	0.48	[238]
140b	130 [a]	0.65	0.52	[238]
141a	280 [a]	1.7	0.75	[61]
141b	340 [a]	0.38	1.8	[61]
141c	265 [a]	1.1	0.93	[61]
142	295 [a]	0.8	0.85	[61]
143	250 [a]	0.93	0.81	[238]

[a] pH 6.7, 0.01 M phosphate, 25 °C. [b] pH 7 (0.1 M phosphate, 5% MeOH). [c] Not recorded.

Very high rates of the HRP-catalyzed (HRP = horse radish peroxidase) oxidation of Ru^{II} into Ru^{III} by H_2O_2 have been measured (Table 7), showing that the cycloruthenated species are also strikingly reactive electron donors for HRP. Two other plant peroxidases from sweet potato (SPP) and

royal palm tree (RPTP) have displayed analogous results, as similar catalytic efficiency in the oxidation of the Ru^{II} complexes were observed. The mediating capacity of the complexes has been evaluated by using the SPP-catalyzed co-oxidation of **49a** and catechol as a poor peroxidase substrate. The rate of enzyme-catalyzed oxidation of catechol increased more than 10,000-fold in the presence of the ruthenium complex.[62]

It should be stressed at this point that the figures reported in Table 7 are among the highest ever reported. This nicely illustrates that the presence of the cycloruthenated unit has had a dramatic effect upon the efficiency of the electron-shuttle behaviour of ruthenium complexes.

6.2. Biological Activity of Cycloruthenated Complexes

The successful use of cycloruthenated complexes as efficient electron shuttles for oxidoreductase enzymes prompted some of us to examine the potential of these compounds for biological applications. Indeed, the study described shortly in the preceding section showed that these organoruthenium derivatives had the required characteristics in order to interact with biomolecules. Several simple ruthenium compounds (see below) are currently being studied for their use as anticancer agents. As cyclometallated compounds of palladium,[239] platinum[240] or gold[241,242] have been shown to display interesting antitumour activity, it seemed worth to test the behaviour of the related cycloruthenated compounds for the same properties. One obvious impetus for these studies is to discover new molecules that would be active against tumour cells and present less harmful side effects than the currently used drugs such as cisplatin. Another important target is to overcome drug resistance induced by cisplatin on several cell lines.

Several research teams with different strategies have described interesting antitumour properties for coordination compounds of Ru^{II} or Ru^{III}, some of them being in phase I or II clinical trial.[243–248] Most of these ruthenium complexes have been built up with more or less weakly bound ligands on the ruthenium atom. None of them was indeed built with ligands strongly bound to the metal such as a cyclometallated ligand. We reasoned that, if our compounds would display any antitumour activity, the fact that the cyclometallated ligand is strongly linked to the ruthenium atom would allow us to have a chance of following the metal in vitro or in vivo. We were thus delighted to observe that several cycloruthenated compounds (Figure 17) from a library of ca. 20 molecules, displayed significantly low IC_{50} concentrations against several tumours such as A-172 cells, for example, derived from a human glioblastoma and cell lines derived from adenocarcinoma (HCT-116) and lymphoma (RDM-4) (Table 8).

These encouraging in vitro data have since been confirmed by in vivo experiments, especially on compound **149**. It was thus shown that the activity of this compound on xenografted tumours (F10B16 mouse melanoma cells and

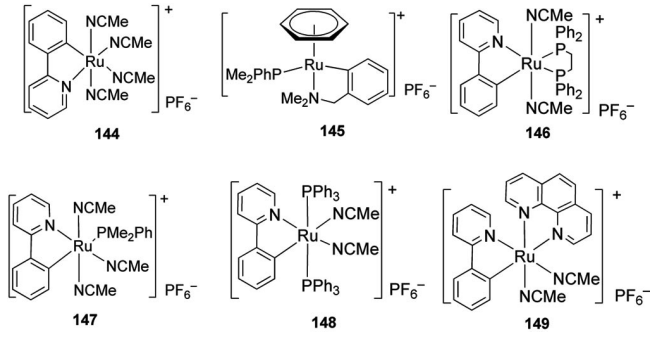


Figure 17. A selection of cycloruthenated compounds whose cytotoxicity has been measured in vitro.

Table 8. IC_{50} [μM] values of the cycloruthenated complexes on three cell lines, taken in part from ref.[63] with permission.

Compounds	Tumour cells			Ref.
	A-172	HCT-116	RDM-4	
cisplatin	3.9 ± 0.2	3 ± 2	3 ± 2	[249]
139b	12 ± 2	10 ± 5	10 ± 5	[63]
144	>50	>50	>50	[249]
145	4.8 ± 0.2	3 ± 2	30 ± 10	[249]
146	1.7 ± 03	3 ± 2	10 ± 5	[249]
147	15 ± 2	5 ± 2	–	[63]
148	3 ± 2	7 ± 2	–	[63]
149	1.9 ± 0.2	3 ± 2	10 ± 5	[249]

U87 human glioblastoma cells) in mice is analogous to the effect of cisplatin (40% reduced growth), the acute toxicity (LD_{50}) was also equivalent to that of cisplatin, but the chronic toxicology (weight loss, kidney and liver toxicity and neurotoxicity) was significantly lower as compared to that of cisplatin.[250] These data allow us to believe that cycloruthenated compounds have a good potential for becoming in some cases substitutes for cisplatin as anticancer drugs, at least for those cancers that developed resistance against cisplatin. However, the mechanism of action of the cycloruthenated compounds is not known yet. They interact with DNA in vitro and cause DNA damage but with less efficiency than cisplatin. In addition, they induce expression of key genes of the reticulum stress signalling pathway. All together, our results showed that the cycloruthenated compounds possess interesting characteristics as compared to cisplatin, including a lower neurotoxicity and the induction of different apoptotic pathways, which suggests they might represent a new or a complementary anticancer chemotherapy.

7. Conclusions

As illustrated in this review, cycloruthenated complexes are important species in many aspects of chemistry or chemical physics. In the near future, it is very likely that other applications will emerge such as their use as molecular sensitizers for dye-sensitized solar cells, which was disclosed very recently.[251] The huge number of ruthenium-containing starting materials that can possibly lead to cy-

cloruthenation through C–H activation is somewhat a burden, as compounds that would be capable of metallating a large library of ligands do not seem to have been identified yet. This is a matter that deserves further research, as the discovery of a versatile cyclometallating complex, playing the same role as palladium acetate for the cyclopalladation reaction, would have valuable consequences in terms of the possibility of applications of these species. For instance, this information will definitely be of interest to synthetic chemists who are looking for powerful C–H activators that work with the assistance of heteroatoms to achieve C–C or C–heteroatom bond formation through green processes.

CCDC-705389 (for **47**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre at http://www.ccdc.ac.uk.data/cif.

Acknowledgments

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