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Cycloaddition of nitrones to free and coordinated (*E*)-cinnamonitrile: effect of metal coordination and microwave irradiation on the selectivity of the reaction

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[2 + 3] Cycloaddition of *N*-methyl-*C*-phenylnitrone to transition metal coordinated (*E*)-cinnamonitrile occurs exclusively at the nitrile C≡N bond, leading to Δ^4-1,2,4-oxadiazoline complexes, from which the heterocyclic ligand can be released and isolated in high yield. In contrast, the reaction of the nitrone with free cinnamonitrile involves the C=C bond only, yielding a diastereomeric mixture of isoxazolidine-4-carbonitriles. Microwave irradiation enhances the reaction rates of both transformations considerably, without changing their regioselectivity with respect to the thermal reactions. The two nitrile ligands in complexes of the type $[MCl_2(cinnamonitrile)_2]$ (M = Pt or Pd) are significantly different in reactivity. Thus, short-time microwave irradiation allows for the selective synthesis of the mono-cycloaddition product $[PtCl_2(cinnamonitrile)(oxadiazoline)]$, even in the presence of an excess of nitrone. Using longer irratiation times, this complex can be further transformed into the bis-cycloaddition product $[PtCl_2(oxadiazoline)_2]$. The latter compound is also produced when thermal heating is applied, however, the formation of the mono-cycloaddition product fails to be selective under thermal conditions.

Introduction

Pericyclic reactions play a predominant role in organic synthesis due to their high atom efficiency and functional group compatibility. Additionally, these reactions can often be influenced by Lewis acids, resulting in modified reactivities and regioselectivities. Chiral Lewis acids are used to induce diastereoselectivity in the cycloaddition reaction, thus offering easy access to enantiomerically pure or enriched carbo- or heterocycles.[1]

In this context, Diels–Alder reactions have been intensively studied, and Lewis acid catalysed versions of this reaction play a key role in the formation of six-membered ring systems in organic synthesis.[2] Dipolar [2 + 3] cycloadditions are one of the most important reactions for the formation of five-membered rings,[3] however, their Lewis acid mediated variants are less frequently and less successfully investigated, since most 1,3-dipolar reagents, or reagents used to generate them *in situ*, are not compatible with the Lewis acid. Metals such as Mg(II), Zn(II), Ti(IV), lanthanides(III), Co(II), Mn(II) were successfully applied as catalysts in selected reactions of nitrones,[4–6] nitrile oxides,[7] or azomethine ylides[8] with C=C bonds. However, most of these reactions still lack general applicability.

In our previous work, we demonstrated that the reaction of nitrones with nitriles is facilitated considerably, and can be performed enantioselectively, if the nitrile is coordinated to a platinum centre.[9] A quantum chemical study of the reaction mechanism showed that bond formation occurs stepwise in presence of a Lewis acid, and the energetic profile of the reaction indicates that the Lewis acid acts by stabilising transition states, intermediates and products rather than by activating the reagents.[10]

In a continuation of this work, we now examined whether a compound such as cinnamonitrile, offering both a C=C and a C≡N bond, would undergo selective cycloaddition at only one of the potentially reactive sites. Since both groups are conjugated, we wondered which functional group would be more reactive, what influence coordination to a metal would have, and in what way a modification of the reaction conditions from classical thermal heating to microwave application would change the product spectrum.

Microwave irradiation is known to influence a large number of cycloadditions, in terms of reaction rates, yields, and occasionally also with respect to selectivities.[11] It is anticipated that mainly cycloadditions with a low degree of concertedness show a significant response to microwave irradiation since the transition states and intermediate are highly polar.[12] A series of [2 + 3] cycloadditions was sucessfully performed using microwave irradiation,[13] including the reaction of nitrones with electron deficient nitriles.[14] However, there are only very few reports on metal-mediated cycloadditions under microwave irradiation up to now.[15]

Results and discussion

Cycloadditions of nitrones with nitriles[10] or electron deficient alkenes[16,17] are considered to occur under HOMO(dipole)–LUMO(dipolarophile) control, and thus, a lowering of the LUMO of cinnamonitrile must be achieved to enhance the reactivity. The Lewis acidic metal must therefore bind to the nitrile rather than to the nitrone's oxygen. Oxophilic Lewis acids like Al, Ti or Zn were thus excluded and transition metals from the platinum group were considered as most appropriate for the purpose of this study. However, unsaturated nitriles can coordinate to platinum metals either *via* the nitrile nitrogen or *via* the alkene. Whereas N-coordination is only rarely observed being more typical for complexes in higher oxidation states,[18] C-coordination seems to occur more frequently in low valent compounds, *e.g.* Pt(0) complexes. The latter coordination mode can lead to either π-complexes[19] or to σ-complexes as a result of insertion into a metal-ligand bond.[20] In the present work, we have chosen the $MCl_2(L)_2$ system as the most promising for the purpose of the study, since the oxidation state of the metal is high enough to favour CN coordination and at the same time to provide sufficient Lewis acid activation. Transition metals in higher oxidation states (*e.g.* of the type $PtCl_4(L)_2$) were excluded because it was feared that the C=C bond would be incompatible with a potential chlorinating agent.

Synthesis of the transition metal cinnamonitrile complexes

The platinum cinnamonitrile complex **1a** was prepared from $PtCl_2(MeCN)_2$ by ligand exchange, using (*E*)-cinnamonitrile as a solvent. For the preparation of the analogous palladium compound **1b**, $PdCl_2$ was dissolved in hot (*E*)-cinnamonitrile and the complex formed was precipitated with diethyl ether.

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Both compounds have the general composition MCl_2-(cinnamonitrile)$_2$, as confirmed by their elemental analysis and mass spectra. The cinnamonitrile coordinates to the metal centre *via* the nitrile nitrogen. This can be concluded from the IR spectra which show a significant shift in the stretching vibration of the C≡N bond (2276 cm^{-1} for the complexes **1a** and **1b**, 2218 cm^{-1} for free cinnamonitrile). The C=C stretch, in contrast, is only moderately affected by the coordination to the metal (1610 cm^{-1} for the Pt complex, 1613 cm^{-1} for the Pd complex, 1621 cm^{-1} for the free cinnamonitrile), indicating that no coordination to the C=C bond occurs. These observations agree well with those made for copper(I) complexes of (*E*)-cinnamonitrile,[21] for which a X-ray structural analysis was performed and the coordination of the ligand *via* its CN group was established. However, in these copper complexes, the CN stretching vibration appears at lower wavenumbers than in the Pt and Pd complexes, showing that the π-backbonding postulated for Cu(I) is less important in the case of Pt(II) and Pd(II).

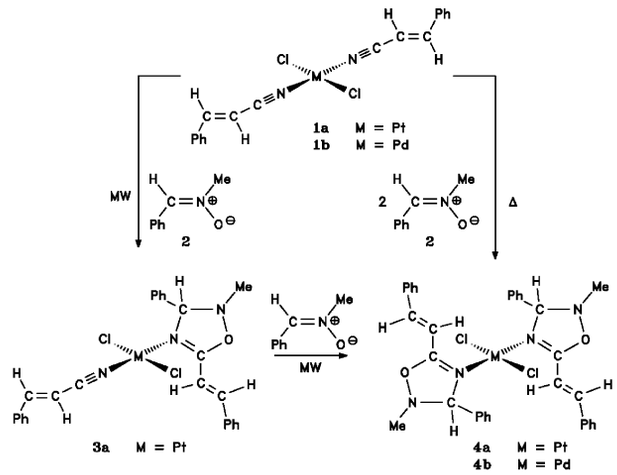
The ^{1}H NMR spectrum of the platinum complex also confirms that the alkene is not coordinated since a similar pattern of signals was obtained as for free cinnamonitrile, but the AB doublets of the alkene protons were shifted downfield due to the electron withdrawing effect of the platinum centre. The appearance of only one set of signals for the organic ligand shows that one isomer of the complex is formed with a high preference. The coupling constant of the alkene protons (16 Hz) is the same as in free cinnamonitrile (16 Hz) and we therefore conclude that the C=C bond in the cinnamonitrile ligand is (*E*)-configured. The organic ligands in the coordination sphere of the transition metal are assumed to be in *trans* position to each other since the complex is very unpolar and shows a similar TLC characteristic as *trans*-[$PtCl_2$(PhCN)$_2$]. A faint spot appearing at a lower R_f value indicates that the corresponding *cis* complex is formed in a minor quantity only.

For the corresponding palladium compound, NMR data are difficult to obtain since the complex decomposes readily in solution in the absence of excess cinnamonitrile. A freshly dissolved sample shows signal patterns very similar to the platinum complex, together with signals of free cinnamonitrile. Additionally, since the IR spectra of the two complexes are almost identical, we conclude that their structure must be analogous.

Cycloaddition reactions to coordinated cinnamonitrile

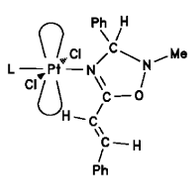
(a) Reaction under thermal conditions. Cycloaddition of *N*-methyl-*C*-phenylnitrone to the cinnamonitrile ligands in **1a** and **1b** is very slow under thermal conditions and requires 2 d at 60 °C for completion (Scheme 1). Cinnamonitrile is thus significantly less reactive than benzonitrile in analogous Pt(II) complexes.[9a,b] The Pt and Pd compounds **1a** and **1b** are similar in reactivity and yield the bis-oxadiazoline complexes **4a** and **4b** as a 1 : 1 mixture of diastereoisomers. The newly formed compounds were characterised by elemental analysis, IR, ^{1}H and ^{13}C{^{1}H} spectroscopy and by FAB-MS spectrometry. Additionally, **4a** was investigated by ^{195}Pt NMR spectroscopy.

Elemental analysis and the mass spectra confirm that the compounds are 2 : 1 adducts of the nitrone with the cinnamonitrile complexes **1a** or **1b**.Their IR, ^{1}H and ^{13}C{^{1}H} spectroscopic data are very similar, showing the structural affinity of the complexes. In the IR spectra, the C≡N stretching vibration disappeared and a strong band for the C=N stretching emerged (1639 cm^{-1} for **4a**, 1647 cm^{-1} for **4b**). The presence of the (*E*)-alkene can be deduced from the appearance of the typical out-of-plane bending vibration (968 cm^{-1} for **4a**, 965 cm^{-1} for **4b**). The ^{195}Pt NMR signal of **4a** is found at −2184 ppm, at a similar position as the signals of previously described [$PtCl_2$(oxadiazoline)$_2$] complexes.[9b] In the ^{1}H and ^{13}C NMR spectra of **4a** and **4b**, all signals of the oxadiazoline ring emerge



Scheme 1 [2 + 3] Cycloaddition of nitrones to Pt(II) or Pd(II)-bound cinnamonitrile under thermal or microwave conditions.

at their expected positions. However, the alkene proton in α-position to the heterocycle is displaced from its normal position at ≈ 6.7 ppm to an unusually high chemical shift (7.40 to 7.50 ppm). The corresponding carbon atom, however, is not affected and appears in the expected range (111.2–112.3 ppm). We therefore conclude that the α-proton is influenced either by the metal centre or by adjacent ligands. If in the preferred conformation the rms plane through the heterocycle and conjugated alkene is orthogonal to the coordination plane around the transition metal, the alkene proton in α-position to the heterocycle comes in close neighbourhood of the transition metal's d_{z^2} orbital (see Scheme 2). This can lead to a drastic change of the ^{1}H chemical shift due to magnetic deshielding or a possible agostic interaction between the proton and the metal centre. On the other hand, if the heterocycle rotates around the metal–nitrogen bond, the corresponding alkene proton approximates the lone pairs located at the chlorine ligands, equally leading to a deshielding.



Scheme 2 Possible conformation and d_{z^2}-interaction of the heterocycle.

(b) Reaction under microwave irradiation. If the cycloaddition to $PtCl_2$(cinnamonitrile)$_2$ **1a** is performed under microwave irradiation, the formation of the bis-oxadiazoline complex **4a** is complete within 2 h. Although this reaction time might appear unusually long for microwave reactions which often take place within a few minutes, the improvement relative to the thermal conditions (2 d under otherwise comparable conditions) is considerable. The product is obtained in similar yield and an unchanged diastereomeric ratio of 1 : 1.

Short-term microwave irradiation (20 min) of a suspension of nitrone **2** and $PtCl_2$(cinnamonitrile)$_2$ in dichloromethane results in selective formation of the mono-cycloaddition product **3a**, independently whether one equivalent or a five-fold excess of nitrone is used. In this product, only one of the CN triple bonds reacted with the nitrone in a [2 + 3] cycloaddition to give the corresponding coordinated oxadiazoline. The second cinnamonitrile ligand is left intact.

The compound was characterised by elemental analysis, FAB-MS, IR, ^{1}H, ^{13}C{^{1}H} and ^{195}Pt NMR spectroscopy. Elemental analysis and the mass spectrum confirm that only one equivalent of the nitrone was introduced into the molecule.

In the IR spectrum, both C≡N and C=N stretching vibrations are visible (2270 cm^{-1} and 1642 cm^{-1}). The C≡N vibration appears at slightly lower wavenumbers than in the starting bis-cinnamonitrile complex **1a**, indicating that the platinum centre acts as a weaker Lewis acid once the first cycloaddition has occured. In the ^{1}H and ^{13}C NMR, the expected signals of both ligands appear at chemical shifts similar to those in the starting complex **1a** and the bis-cycloaddition product **4a**. The chemical shifts of the alkene of the cinnamonitrile ligand are in between the corresponding values for the cinnamonitrile complex **1a** and the uncoordinated cinnamonitrile, confirming the reduced influence of the Pt centre. The alkene of the oxadiazoline ligand shows an unusually high chemical shift for the proton in α-position to the heterocycle (7.49 ppm), just as in the bis-cycloaddition product. This indicates that this proton interacts in the same way with the metal centre or the chlorine ligands, as shown in Scheme 2. The ^{195}Pt resonance at −2268 ppm is in between the values found for the bis-cycloaddition product **4a** and the expected position of $[PtCl_2(nitrile)_2]$ complexes.[22]

The fact that the mono-cycloaddition product is formed selectively is attributed to the different extent of Lewis acid activation the platinum centre exhibits. In the starting complex $[PtCl_2(cinnamonitrile)_2]$, the Pt centre is a stronger Lewis acid, because all coordinated ligands, Cl as well as the nitriles, are electron withdrawing, and this is expected to result in a high activation of the C≡N bond. After the first cycloaddition, the coordination sphere around the platinum atom consists of two chlorine, one nitrile and one oxadiazoline ligand. The oxadiazoline ligand is less electron withdrawing than a nitrile, and therefore, the Lewis acidity of the platinum atom is reduced and the activation of the remaining nitrile ligand is weaker. The effect on the reactivity of the C≡N bond is quite pronounced because both oxadiazoline and nitrile are in *trans* position to each other where the electronic communication between them is strongest.

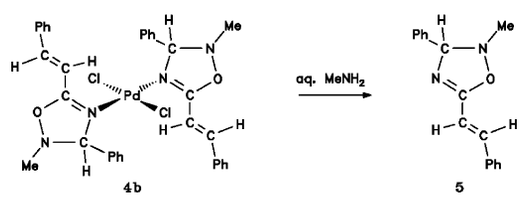
When the cycloaddition was performed under thermal conditions in a NMR tube and monitored, the mono-cycloaddition product **3a** was detected as an intermediate product. However, this product could not be prepared selectively under thermal conditions. Instead, a mixture of starting material, mono- and bis-cycloaddition products was obtained. This lack of selectivity of the thermal reaction might arise from two essentially different reasons: Since the starting cinnamonitrile complex is poorly soluble in CH_2Cl_2, the small amount present in solution faces a high excess of nitrone, and therefore the reaction to the bis-cycloaddition product is favoured. In microwave conditions, heating of the sample is faster and superheating of the solvent can occur, both supporting the dissolution process and favouring a reaction in a homogenous phase. On the other hand, microwave irradiation might indeed result in a better differentiation between the two nitrile ligands in the complex if the transition states involved in the individual cycloadditions are different in polarity. This is much likely to be the case since the Lewis acidity of the platinum center decreases in the course of the reaction. As a consequence, the first cycloaddition has a higher tendency towards a two-step reaction *via* highly polar transition states and an intermediate. The second cycloaddition comes closer in mechanism to a concerted reaction. Its transition state is less polar and therefore less susceptible to microwaves.

In conclusion, the cycloaddition of nitrones to the C≡N bond of transition metal bound cinnamonitrile is not only considerably faster under microwave conditions but also significantly more selective. It thus allows for the preparation of transition metal complexes which are otherwise not accessible, if thermal conditions are applied.

(c) Reaction under forcing conditions and excess of nitrone. The cycloaddition to the platinum cinnamonitrile complex **1a** was also attempted under more forcing conditions, with the aim to achieve a reaction with both C≡N and C=C bonds of the ligand. However, reaction with even a five-fold excess of nitrone only produced the known bis-oxadiazoline complex **4a** as the product of cycloaddition to the two CN bonds. No reaction with the alkene took place, independent whether thermal or microwave conditions were applied. If the reaction was continued using more drastic reaction conditions (140 °C, 2 h, microwave, or 60 °C, 3 weeks, thermal heating) under which free cinnamonitrile underwent cycloaddition at the C=C bond (see last section), the platinum oxadiazoline complex rather decomposed but did not undergo further cycloaddition. These results indicate that the C=C bond is not sufficiently activated by the presence of the metal. Additionally, one can conclude that an alkene conjugated to an oxadiazoline is less reactive in the cycloaddition with nitrones than a nitrile conjugated one. Oxadiazolines, even when metal-coordinated, are less electron withdrawing than a nitrile.

Release of the ligand

The newly formed oxadiazoline **5** was released from the corresponding palladium complex **4b** upon reaction with aqueous methylamine, and isolated by chromatography (Scheme 3). The platinum complex **4a** can also be used for this reaction, however, the release of the ligand is significantly slower (5 h) than in the case of the palladium complex (10 min).



4b 5

Scheme 3 Displacement of the oxadiazoline ligand from the metal.

The oxadiazoline **5** was characterised by IR, ^{1}H and $^{13}C\{^{1}H\}$ NMR spectroscopy and accurate EI-MS spectrometry. The mass spectrum identifies the compound as a 1 : 1 adduct of cinnamonitrile with the nitrone. The IR spectrum shows the presence of a strong C=N stretching vibration at 1656 cm^{-1} and the absence of the respective band for a C≡N bond. The presence of the *trans*-HC=CH moiety is reflected in the IR spectrum (HC=CH out of plane bending at 972 cm^{-1}), the characteristic pair of doublets with a coupling constant of 16 Hz at chemical shifts of 6.71 and 7.45 ppm in the ^{1}H NMR, and the typical signals in $^{13}C\{^{1}H\}$ NMR at 112.9 and 141.9 ppm.

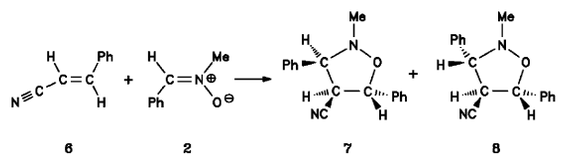
As compared to the complexes, the free ligand displays its C=N vibration at higher wavenumbers, indicating that the double bond character of the imino group becomes more pronounced upon release from the metal. In the ^{1}H NMR spectrum, the signals of the alkene are shifted back to their expected position since the influence of the metal and its coordination sphere is no longer present. All other NMR signals are only weakly displaced with respect to their position in the complex.

Cycloaddition reactions of free cinnamonitrile

Unsaturated nitriles are known to undergo cycloadditions preferentially at the C=C bond, without affecting the C≡N bond. Acrylonitrile, for example, reacts with nitrones to give two regioisomeric isoxazolidines, and no cycloaddition to the nitrile was observed.[23] In the reaction of cinnamonitrile with arylnitrile oxides, the C=C cycloaddition products are usually formed as major products, and only a minor quantity of the CN cycloaddition product is found.[24] Aminocinnamonitriles bearing a NR_2 group behave similarly, however, if the amino function contains a hydrogen substituent, the reaction at the C≡N can become predominant.[24]

In order to compare the results of the metal mediated reaction with the uncatalysed one, the reaction of free

cinnamonitrile with *N*-methyl-*C*-phenylnitrone was examined. A similar study using other nitrones was published already,[25] but only thermal reaction conditions were applied. Cinnamonitrile is less reactive than acrylonitrile in cycloadditions with nitrones. With nitrone **2**, a moderate conversion of 30% was achieved at 60 °C under solvent-free conditions over a period of three weeks or upon microwave irradiation for 2 h at 100 °C (Scheme 4). Two diastereomeric isoxazolidines **7** and **8** are formed in a 1 : 1 ratio, both arising from addition of the nitrone to the C=C bond, leaving the nitrile intact. With this, the chemoselectivity of the cycloaddition is switched with respect to the exclusive CN attack in the metal-mediated reaction.



Scheme 4 [2 + 3] Cycloaddition of nitrones to free cinnamonitrile under thermal or microwave conditions.

If the reaction is performed at higher temperature (either thermally or by irradiation with microwaves), formation of uncharacterised by-products is observed, without driving the reaction to a higher conversion. A change from solvent-free conditions in the microwave reaction to the use of CH_2Cl_2 or toluene as a solvent gives comparable results in terms of conversion and isomeric composition of the product but no improvement.

The two diastereomeric products **7** and **8** were separated by chromatography and analysed by IR, ^{1}H and ^{13}C{^{1}H} NMR spectroscopy and accurate EI-MS spectrometry. The IR spectra are almost identical, indicating that the compounds are diastereoisomers rather than regioisomers. Both compounds show the typical coupling pattern of a CH(R)–CH(R′)–CH(R″) moiety in the ^{1}H NMR spectrum. Their stereochemistry was established with the help of NOESY spectra. Isomer **7** reveals a strong NOE between the N–CH group and a phenyl group, and additionally between the N–CH and the adjacent CH–CN group. This indicates that the protons in the respective groups must be *cis* to each other. In contrast, the O–CH proton shows an NOE to aromatic signals but not to the CH–CN, the ring protons must therefore be *trans* to each other. In isomer **8** the CH–CN exhibits an NOE to two different signals in the aromatic range but not to the N–CH or O–CH groups. In addition, the N–CH and O–CH show an NOE to one of the aromatic signals each. This is consistent with **8** being the (*trans*, *trans*)-2-methyl-3,5-diphenylisoxazolidine-4-carbonitrile.

The other pair of possible regioisomers in which the nitrone oxygen is bound to the CH–CN (isoxazolidine-5-carbonitriles) was not detected, in analogy to results of a previous study using other nitrones.[25] We assume that these isomers do not form due to steric repulsion of the two phenyl groups in the transition state. A detailed computational study analysing the selectivities of this rection under thermodynamic and kinetic control is underway in our group.

Concluding remarks

We showed in this work that the selectivity of the cycloaddition of nitrones to cinnamonitrile can be switched from a pure C=C attack to an exclusive C≡N attack if the cinnamonitrile is coordinated to a transition metal such as Pt or Pd. With this, the product spectrum can be changed from oxazolidines to oxadiazolines. The newly formed oxadiazoline ligand can be released from the metal, thus offering a synthetic route to heterocycles which are otherwise not accessible in organic chemistry.

Under microwave irradiation, both metal-mediated and metal-free reactions are accelerated considerably, without changing their chemo- and regioselectivities relative to the thermal reactions. However, in addition to the enhanced reaction rates, microwave irradiation also renders the reaction with symmetric transition metal complexes of the type MCl_2(nitrile)$_2$ significantly more selective, thus achieving a reaction of only one of the like ligands without affecting the other one. The method therefore allows for the preparation of unsymetrically substituted transition metal complexes which are otherwise not accessible, if thermal conditions or other synthetic methods were applied. An extension of this subtle differentiation in reactivity to reactions other than cycloadditions or other ligands might give general access to a large variety of non-symmetric transition metal complexes for a diversity of applications.

Experimental

Materials and instrumentation

Solvents were obtained from commercial sources and used as received. [$PtCl_2(MeCN)_2$][26] and *N*-methyl-*C*-phenylnitrone[27] were prepared according to published methods. Microwave experiments were performed in a Smith Creator™ microwave reactor (Personal Chemistry, Uppsala) in 0.5 to 2 ml Pyrex glass tubes which were septum sealed with a pressure release cap. C, H and N elemental analyses were carried out on a Leeman CE 440 automatic analyser. Infrared spectra (4000–400 cm^{-1}) were recorded on Perkin Elmer 2000 FTIR and Nicolet Avatar 320 FT-IR spectrometers in KBr pellets. Positive FAB-MS spectra of the samples in 3-nitrobenzyl alcohol (NBA) matrices were obtained on a Finnigan MAT 900XLT instrument. Accurate EI-MS spectra were recorded on a Thermoquest MAT 95XL instrument, using perfluorokerosine (PFK) as reference. ^{1}H, ^{13}C{^{1}H} and ^{195}Pt NMR experiments were acquired on Bruker DRX 500 and Bruker AMX 300 spectrometers at ambient temperature. Signals in ^{1}H and ^{13}C were assigned with the help of COSY, NOESY and HMQC spectra. ^{195}Pt chemical shifts are given relative to aqueous $K_2[PtCl_4]$ = −1630 ppm, with half height line widths in parenthesis.

Preparation of the transition metal cinnamonitrile complexes

***trans*-[$PtCl_2${N≡C–CH=CHPh}$_2$].** A suspension of *cis*/*trans*-$PtCl_2(MeCN)_2$ (300 mg, 0.86 mmol) in (*E*)-cinnamonitrile (1.5 ml) was heated to 60 °C for one week whereupon the yellow finely dispersed starting complex was transformed into a crystalline yellow solid. After addition of diethyl ether (10 ml), the solid was filtered off, washed with diethyl ether and dried in air.

Yield 81%. Anal. Calc. for $C_{18}H_{14}Cl_2N_2Pt$: C, 41.23; H, 2.69; N, 5.34. Found: C, 41.57; H, 2.45; N, 5.36%. FAB$^+$-MS, *m*/*z*: 523 [M]$^+$. IR spectrum (selected bands), cm^{-1}: 3010w *ν*(C–H), 2276m *ν*(C≡N), 1610m *ν*(C=C), 965m *γ*(*trans*-HC=CH). ^{1}H NMR ($CDCl_3$): *δ* 6.17 (d, 16.0 Hz, 1H, =CH–CN), 7.45–7.53 (m, 5H, Ph), 7.69 (d, 16.0 Hz, 1H, =CH–Ph). ^{13}C and ^{195}Pt NMR data were not obtained due to the low solubility of the complex in all common NMR solvents.

***trans*-[$PdCl_2${N≡C–CH=CHPh}$_2$].** A suspension of $PdCl_2$ (100 mg, 0.56 mmol) in (*E*)-cinnamonitrile (0.5 ml) was heated to 60 °C for two weeks until the dark $PdCl_2$ was completely dissolved. Diethyl ether was added, the orange solid was filtered off, washed with diethyl ether and dried in air.

Yield 68%. Anal. Calc. for $C_{18}H_{14}Cl_2N_2Pd$: C, 49.63; H, 3.24; N, 6.43. Found: C, 49.77; H, 3.09; N, 6.37%. FAB$^+$-MS in cinnamonitrile, *m*/*z*: 309 [M]$^+$. IR spectrum (selected bands), cm^{-1}: 3010w *ν*(C–H), 2276m *ν*(C≡N), 1613m *ν*(C=C), 965m *γ*(*trans*-HC=CH). ^{1}H NMR ($CDCl_3$): *δ* 6.03 (d, 16.0 Hz, 1H, =CH–CN), 7.41–7.52 (m, 5H, Ph), 7.66 (d, 16.0 Hz, 1H, =CH–Ph). ^{13}C NMR data were not obtained due to rapid decomposition of the complex in solution.

Preparation of the transition metal oxadiazoline complexes

***trans*-[$PtCl_2${N=C(CH=CHPh)O–N(Me)–CH(Ph)}$_2$].**

(a) Thermal reaction. A mixture of *trans*-[$PtCl_2${N≡C–CH=CHPh}$_2$] (26 mg, 0.05 mmol) and *N*-methyl-*C*-phenylnitrone (27 mg, 0.20 mmol) in CH_2Cl_2 (2 ml) was placed in a closed tube and left at 60 °C for 2 days. The yellow solution was filtered through a pad of silica gel. After evaporation of the solvent the product was crystallised by slow evaporation of a solution of CH_2Cl_2 and diethyl ether.

(b) Microwave reaction. A mixture of *trans*-[$PtCl_2${N≡C–CH=CHPh}$_2$] (26 mg, 0.05 mmol) and *N*-methyl-*C*-phenylnitrone (27 mg, 0.20 mmol) in CH_2Cl_2 (2 ml) was placed into a Pyrex glass reaction tube and irradiated with microwaves for 2 h at a set temperature of 100 °C. The yellow solution was filtered through a pad of silica gel. After evaporation of the solvent and trituration of the yellow oil with diethyl ether, the product was obtained as a pale yellow solid.

Two diastereoisomers in a 1 : 1 ratio. Yield 35% (method a), 30% (method b). Anal. Calc. for $C_{34}H_{32}Cl_2N_4O_2Pt$: C, 51.39; H, 4.06; N, 7.05. Found: C, 50.21; H, 3.73; N, 6.95%. FAB$^+$-MS, *m*/*z*: 817 $[M + Na]^+$, 723 $[M - 2Cl]^+$. IR spectrum (selected bands), cm^{-1}: 3054m *ν*(C–H), 1639s *ν*(C=N), 1595m *ν*(C=C), 968m *γ*(*trans*-HC=CH). ^{1}H NMR ($CDCl_3$): *δ* 2.96 (s, 3H, NMe), 5.89 and 5.98 (two s, 1H, two diastereomeric N–CH–N), 7.50, 7.58, 7.40 and 7.55 (2H, HC=CH of the two diastereomers), 7.38–7.61 (m, 8H, Ph) and 7.71 (m, 2H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$): *δ* 46.2 (NMe), 91.9 (N–CH–N), 111.2 and 111.3 (CH=), 144.7 and 144.8 (CH=), 128.1, 128.2, 128.4, 128.58, 128.6, 128.9, 129.0, 129.3, 129.33 and 131.0 (two Ph), C=N not detected. ^{195}Pt NMR ($CDCl_3$): *δ* −2184 (750 Hz).

***trans*-[$PdCl_2${N=C(CH=CHPh)O–N(Me)–CH(Ph)}$_2$].** A suspension of *trans*-[$PdCl_2${N≡C–CH=CHPh}$_2$] (50 mg, 0.16 mmol) and *N*-methyl-*C*-phenylnitrone (47 mg, 0.35 mmol) in cinnamonitrile (0.5 ml) was heated to 60 °C for two days whereupon a clear orange solution had formed. The product was precipitated with diethyl ether as a pale yellow powder which was filtered off and dried in air.

Yield is 68%. Anal. Calc. for $C_{34}H_{32}Cl_2N_4O_2Pd$: C, 57.85; H, 4.57; N, 7.94. Found: C, 57.51; H, 4.66; N, 7.52%. FAB$^+$-MS, *m*/*z*: 669 $[M - Cl]^+$. IR spectrum (selected bands), cm^{-1}: 3060m *ν*(=C–H), 1647s *ν*(C=N), 1625m *ν*(C=C), 965m *γ*(*trans*-HC=CH). ^{1}H NMR ($CDCl_3$): *δ* 2.94 (s, 3H, NMe), 5.83 (s, 1H, N–CH–N), 7.46 (d, 16.1 Hz, 1H, CH=), 7.68 (d, 16.0 Hz, 1H, CH=), 7.30–7.50 (m, 8H, Ph) and 7.66 (d, 7.4 Hz, 2H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$): *δ* 46.7 (NMe), 92.0 (N–CH–N), 112.3 (CH=), 126.2, 128.2, 128.8, 128.9, 129.2, 131.2, 134.8 and 142.4 (two Ph), 145.5 (CH=), 163.3 (broad, C=N).

***trans*-[$PtCl_2${N=C(CH=CHPh)O–N(Me)–CH(Ph)}{N≡C–CH=CHPh}].** Mono-cycloaddition in microwave conditions: a mixture of *trans*-[$PtCl_2${N≡C–CH=CHPh}$_2$] (26 mg, 0.05 mmol) and *N*-methyl-*C*-phenylnitrone (6 mg, 0.05 mmol) in CH_2Cl_2 (2 ml) was placed into a Pyrex glass reaction tube and irradiated with microwaves for 20 min at a set temperature of 100 °C. The yellow solution was filtered through a pad of silica gel, the solvent was evaporated and the residual yellow oil triturated with diethyl ether to precipitate the product as a pale yellow solid.

Yield 40%. Anal. Calc. for $C_{26}H_{23}Cl_2N_3OPt$: C, 47.35; H, 3.52; N, 6.37. Found: C, 47.60; H, 3.61; N, 6.34%. FAB$^+$-MS, *m*/*z*: 682 $[M + Na]^+$, 623 $[M - Cl]^+$, 588 $[M - 2Cl]^+$. IR spectrum (selected bands), cm^{-1}: 3055w *ν*(=C–H), 2270w *ν*(C≡N), 1642s *ν*(C=N and C=C), 967m *γ*(*trans*-HC=CH). ^{1}H NMR ($CDCl_3$): *δ* 3.00 (s, 3H, NMe), 5.95 (s, 1H, N–CH–N), 6.03 (d, 16 Hz, CH=, nitrile), 7.54 (d, 16 Hz, 1H, CH=, nitrile), 7.49 (d, 16 Hz, 1H, CH=, oxadiazoline), 7.64 (d, 16 Hz, 1H, CH=, oxadiazoline), 7.30–7.38 (m, 13H, Ph) and 7.57–7.62 (m, 2H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$): *δ* 46.7 (NMe), 92.1 (N–CH–N), 93.7 (CH=, nitrile), 156.3 (CH=, nitrile), 111.0 (CH=, oxadiazole), 146.3 (CH=, oxadiazole), 127.8, 128.1, 128.5, 128.8, 129.1, 129.3, 129.4, 129.5, 129.9, 131.3, 132.6 and 134.0 (three Ph), C=N not detected. ^{195}Pt NMR ($CDCl_3$): *δ* −2268 (750 Hz).

Displacement of the oxadiazoline from the palladium complex

{N=C(CH=CHPh)O–N(Me)–CH(Ph)}. To a solution of *trans*-[$PdCl_2${N=C(CH=CHPh)O–N(Me)–CH(Ph)}$_2$] (50 mg, 0.071 mmol) in $CHCl_3$ (1 ml), an excess of an aqueous solution of methylamine (0.2 ml, 40% solution) was added and the reaction mixture stirred at 50 °C for 10 min. The organic phase was separated and passed through a pad of silica gel. After evaporation of the solvent, the product was obtained as colourless oil which solidified upon standing.

Yield 88%. Accurate EI-MS, *m*/*z*: Calc. for $C_{17}H_{16}N_2O$: 264.1257. Found: 264.1256 (Δ[mmu] −0.1). IR spectrum (selected bands), cm^{-1}: 3062w and 3029w *ν*(=C–H), 1656s *ν*(C=N and C=C), 972m *γ*(*trans*-HC=CH). R_f (SiO_2/CH_2Cl_2): 0.31. ^{1}H NMR ($CDCl_3$): *δ* 2.94 (s, 3H, NMe), 5.68 (s, 1H, N–CH–N), 6.71 (d, 16.3 Hz, 1H, CH=), 7.45 (d, 16.3 Hz, 1H, CH=), 7.31 (t, 7.2 Hz, 1H), 7.37 (m, 5H), 7.43 (d, 7.2 Hz, 2H) and 7.50 (d, 7.2 Hz, 2H)(two Ph). ^{13}C{^{1}H} NMR ($CDCl_3$): *δ* 47.2 (NMe), 93.9 (N–CH–N), 112.9 (CH=), 126.7, 127.8, 128.6, 128.8, 129.2, 130.2, 135.1 and 140.0 (two Ph), 141.9 (CH=), 160.4 (C=N).

Cycloaddition of *N*-methyl-*C*-phenylnitrone to (*E*)-cinnamonitrile

(a) Thermal reaction. A mixture of (*E*)-cinnamonitrile (65 mg, 0.5 mmol) and *N*-methyl-*C*-phenylnitrone (68 mg, 0.5 mmol) was heated to 60 °C for three weeks. The products **7** and **8** were isolated by column chromatography on silica gel/CH_2Cl_2/hexane 4:1 and obtained as colourless oils.

(b) Microwave reaction. A mixture of (*E*)-cinnamonitrile (100 mg, 0.8 mmol) and *N*-methyl-*C*-phenylnitrone (406 mg, 3.0 mmol) in CH_2Cl_2 (0.5 ml) was irradiated with microwaves for 2 h at a set temperature of 100 °C. The products **7** and **8**, were isolated by column chromatography on silica gel/CH_2Cl_2/hexane 4 : 1 and obtained as colourless oils.

{N≡C–CH–CH(Ph)–O–N(Me)–CH(Ph)}. Two diastereomers in a 1 : 1 ratio. Yield 30% (method a), 30% (method b).

rac-(3*S*, 4*R*, 5*S*)-2-Methyl-3,5-diphenylisoxazolidine-4-carbonitrile **8**: accurate EI-MS, *m*/*z*: Calc. for $C_{17}H_{16}N_2O$: 264.1257. Found: 264.1257 (Δ[mmu] 0.0). IR spectrum (selected bands), cm^{-1}: 3034w, 2964w *ν*(=C(H), 2245w *ν*(C≡N). R_f (SiO_2/CH_2Cl_2/hexane 4 : 1): 0.48. ^{1}H NMR ($CDCl_3$): *δ* 2.75 (s, 3H, NMe), 3.43 (dd, 9.2 Hz, 6.6 Hz, 1H, CH–CN), 3.99 (d, 9.3 Hz, 1H, CHPh–N), 5.41 (d, 6.6 Hz, 1H, CHPh–O), 7.34 (m, 1H), 7.41 (t, 7.5 Hz, 2H) and 7.51 (d, 7.0 Hz, 2H)(Ph–CHN), 7.39–7.39 (m, 5H, Ph–CHO). ^{13}C{^{1}H} NMR ($CDCl_3$): *δ* 43.1 (NMe), 51.1 (CH–CN), 77.5 (CHPh–N), 81.0 (CHPh–O), 118.1 (C≡N), 125.6 ($CH_{o,m}$), 127.3 ($CH_{o,m}$), 128.4 (CH_p), 128.9 ($CH_{o,m}$), 129.2 (CH_p and $CH_{o,m}$), 134.8 (C_q) and 140.1 (C_q) (two Ph).

rac-(3*R*, 4*R*, 5*S*)-2-Methyl-3,5-diphenylisoxazolidine-4-carbonitrile **7**: accurate EI-MS, *m*/*z*: Calc. for $C_{17}H_{16}N_2O$: 264.1257. Found: 264.1258 (Δ[mmu] 0.3). IR spectrum (selected bands), cm^{-1}: 3065w, 3034w, 2964w, 2877w *ν*(=C(H), 2245w *ν*(C≡N). R_f (SiO_2/CH_2Cl_2/hexane 4 : 1): 0.45. ^{1}H NMR ($CDCl_3$): *δ* 2.73 (s, 3H, NMe), 3.56 (dd, 9.0 Hz, 7.1 Hz, 1H, CH–CN), 3.92 (d, 9.0 Hz, 1H, CHPh–N), 5.33 (d, 7.1 Hz, 1H, CHPh–O), 7.38–7.48 (m, 10H, two Ph). ^{13}C{^{1}H} NMR ($CDCl_3$): *δ* 43.2 (NMe), 49.3 (CH–CN), 75.1 (CHPh–N), 82.9 (CHPh–O), 117.9 (C≡N), 125.8 ($CH_{o,m}$), 128.7 ($CH_{o,m}$), 129.1 ($CH_{o,m}$), 129.2 ($CH_{o,m}$), 129.4 (CH_p), 129.5 (CH_p), 134.7 (C_q) and 137.1 (C_q) (two Ph).

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