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Note

Reactions of nitrones with transition metal nitrile complexes: cycloaddition, ligand substitution, or hydrolysis

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Abstract

The reaction of nitrones with transition metal nitrile complexes of the type $[MCl_2(PhCN)_2]$ and $[MCl_4(MeCN)_2]$ leads to different products, depending on the metal. Reaction of $[PdCl_2(PhCN)_2]$ with RCH=N(Me)O (R = Ph, p-C_6H_4Me) afford Δ^4-1,2,4-oxadiazoline complexes $[PdCl_2\{\overline{N{=}C(Ph)O{-}N(Me)C}H(R)\}_2]$ as products of [2 + 3] cycloaddition of the nitrone across the C≡N bond of the nitrile. The oxophilic transition metal compounds $[TiCl_4(MeCN)_2]$ and $[ZrCl_4(MeCN)_2]$ undergo rapid ligand exchange to form nitrone complexes from which the nitrone can be released without decomposition. The closely related compounds $[MoCl_4(MeCN)_2]$ and $[WCl_4(MeCN)_2]$ mediate the hydrolysis of nitrones to the corresponding aldehydes.

Keywords: Cycloaddition; Oxadiazoline complex; Nitrone complex; Nitrone hydrolysis

1. Introduction

Reactions of coordinated ligands [1] play an important role in both inorganic and organic chemistry. New functional group transformations can be achieved which extend and complement the synthetic possibilities of organic chemistry. Additionally, the modified ligand reactivity can provide information about bonding properties, electronic and steric influence of the metal and adjacent ligands, or the reactivity of the individual metal center itself, thus contributing to a deeper understanding of inorganic aspects of chemistry.

In our previous work, we found that platinum in oxidation states +2 or +4 mediates the cycloaddition of aliphatic and aromatic nitrones to the C≡N bond of the coordinated nitrile to give Δ^4-1,2,4-oxadiazoline complexes from which the newly formed heterocycle can be released and isolated [2–4]. Pt(IV) has a stronger activating effect than Pt(II) due to its stronger Lewis acidity. The reaction can be applied in the synthesis of heterocycles which are otherwise not accessible in organic chemistry. Additionally, chiral platinum complexes can be used to induce diastereoselectivity into the cycloaddition, thus allowing for the first enantioselective synthesis of Δ^4-1,2,4-oxadiazolines [5].

In order to understand the effect of the platinum center in more detail, a quantum chemical study was performed, using BF_3 as a model Lewis acid [6]. The mechanism of the cycloaddition was found to change from a concerted one to a two-step process; the Lewis acid thereby facilitates the reaction by stabilising transition states and intermediates rather than by activating the reagents. BF_3 models surprisingly well the experimental results obtained with platinum, suggesting that the reaction is indeed Lewis acid mediated and possibly generally feasible with any Lewis acid. In order to test this hypothesis, we now examined other transition metal nitrile complexes with respect to their reactions with nitrones. $[PdCl_2(MeCN)_2]$, $[PdCl_2(PhCN)_2]$, $[TiCl_4(MeCN)_2]$, $[ZrCl_4(MeCN)_2]$, $[MoCl_4(MeCN)_2]$ and $[WCl_4(MeCN)_2]$ were chosen because these complexes are readily available and structurally closely related to the previously studied platinum compounds [2–4]. Depending on the metal, three different reaction modes were observed, as shown in Scheme 1.

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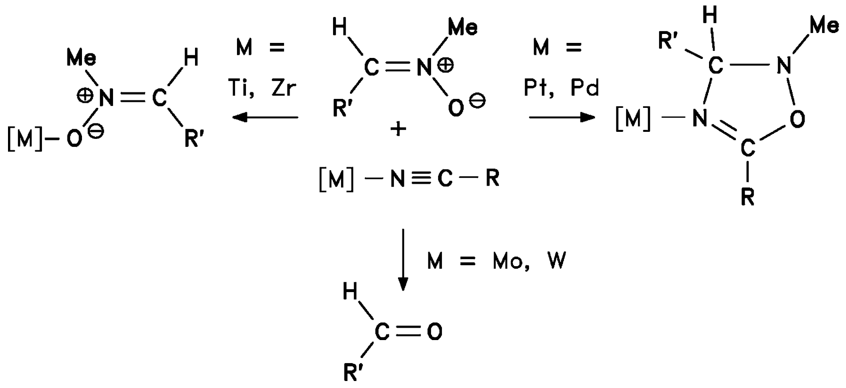

Scheme 1. Reaction of transition metal nitrile complexes with nitrones ($R = Me$, Ph; $R' = Ph$, p-C_6H_4Me).

2. Cycloaddition to the C≡N bond

The reaction of the nitrones $RCH{=}N(Me)O$ ($R = Ph$, p-MeC_6H_4) with $PdCl_2(PhCN)_2$ in PhCN as solvent proceeds smoothly under mild conditions to give the corresponding $PdCl_2(oxadiazoline)_2$ complexes as stable compounds as a result of cycloaddition of the nitrone across the C≡N bond of the coordinated nitrile. This resembles much the behaviour of our previously studied platinum compounds [3], and even in terms of reactivity, there is practically no difference between these two metals. The products were characterised by elemental analysis, mass spectrometry, IR, ^1H and ^{13}C NMR spectroscopy. Elemental analysis and the mass spectrum identify the compounds as adducts of $PdCl_2(PhCN)_2$ with two equivalents of the nitrone. IR and NMR spectroscopic data show the presence of coordinated Δ^4-1,2,4-oxadiazolines and closely resemble those found for the previously described analogous platinum complexes [3,4].

However, the use of the parent nitrile as a solvent is essential, in order to achieve a cycloaddition. Our attempts to prepare palladium(II) oxadiazoline complexes *via* cycloaddition of nitrone to $PdCl_2(PhCN)_2$ in CH_2Cl_2 or $CDCl_3$ failed. Only mixtures of unidentified products were produced, and no evidence for the formation of free or coordinated oxadiazolines was obtained. This is quite in contrast to the behaviour of the platinum compounds, which tolerate a large variety of solvents without any alteration of the reactivity. We assume that this difference is due to the instability of the palladium nitrile complex in solution. It is known that $PdCl_2(PhCN)_2$ disproportionates in absence of the parent nitrile to give the chloro-bridged dimer $[PdCl_2(PhCN)]_2$ and free PhCN in equilibrium [7]. In the dimeric compound, the metal acts as a weaker Lewis acid and therefore, the coordinated nitrile is not reactive enough to undergo cycloaddition.

The reaction of $[PdCl_2(PhCN)]_2$ with an excess of nitrone in benzonitrile as a solvent did not produce any free oxadiazoline, indicating that the reaction is not catalytic but in fact metal mediated, in spite of the higher kinetic lability of palladium with respect to platinum. This agrees well with the results of our theoretical study [6], which revealed a much stronger interaction of the Lewis acid with the transition states, intermediate and product than with the starting material. With this, the reaction is promoted because of its higher thermodynamic driving force and lower activation barrier, but at the same time, the reaction becomes product inhibited.

Although the cycloaddition is not catalytic, the palladium route might still offer advantages in the synthesis of Δ^4-1,2,4-oxadiazolines since the subsequent release of the heterocycle from the metal is significantly faster than in the case of platinum complexes, due to the higher kinetic lability of palladium. Thus, displacement of the oxadiazoline ligands by aqueous ethane-1,2-diamine is complete within 10 min, as compared to several days when platinum complexes are used.

It is worthwhile to mention that the closely related complex $PdCl_2(MeCN)_2$ is unreactive towards nitrones, even if more drastic reaction conditions (80 °C, 1 week) are applied. This again agrees with previous observations with the corresponding platinum compound. The transition metal in a moderate oxidation state +2 is not able to activate acetonitrile sufficiently, but a higher oxidation state is required.

3. Formation of nitrone complexes

In order to compare the reactivity of the previously studied platinum(IV) acetonitrile complexes [2] with other transition metal compounds in high oxidation state, the reaction of $[TiCl_4(MeCN)_2]$ and $[ZrCl_4(MeCN)_2]$ with nitrones was examined. In contrast to our expectations, the nitriles in these complexes do not undergo cycloaddition but substitution of the nitrile for nitrone was observed, even if the parent nitrile was used as a solvent.

Addition of the nitrone to a solution of $[TiCl_4(MeCN)_2]$ or $[ZrCl_4(MeCN)_2]$ in acetonitrile at room temperature results in an immediate precipitation of a colourless solid. This material is highly insoluble in organic solvents, thus preventing analysis by mass spectrometry or by NMR spectroscopy in solution. The elemental analyses vary from batch to batch but reveal a constant C,H,N ratio consistent with the one expected for the individual nitrones. Assuming a general formula $[MCl_4(\text{nitrone})_n]$, the content of nitrone n typically varies from 1.3 to 1.8. Compounds of such composition can be formed by exchange of the nitrile for nitrones and concomitant aggregation to form chlorine or oxygen bridged polynuclear species. A polymeric structure is also consistent with the low solubility and high melting points (>250 °C) of the products.

The IR spectrum confirms this interpretation insofar as no stretching vibration in the typical range of a C≡N bond appears. Instead, the vibrational pattern of the nitrone is observed, with a strong band for a C=N stretching at 1604–1612 cm^{-1} and a strong stretching vibration of the N–O bond at 1156–1160 cm^{-1}. Compared to the free nitrone, the C=N band in the complex is weakly displaced to higher wavenumbers (approx. 10–15 cm^{-1}), indicating a more pronounced double bond character of this bond. At the same time, the N–O vibration is shifted to the opposite direction by approx. 10 cm^{-1}, thus accounting for a weakening of this bond in the complex. These trends are expected if the nitrone is oxygen-bound to the metal.

If the isolated Ti or Zr compounds are suspended in $CDCl_3$ and shaken with D_2O, rapid dissolution occurs. NMR analysis of the aqueous phase shows that there is no MeCN released from the complexes. The nitrone is the only product detected in the organic phase, no oxadiazoline was found. This again confirms that the nitrone substituted the weakly bound nitrile to give a stable nitrone complex.

Nitrone complexes are not much common in coordination chemistry, but were postulated as intermediates in metal catalysed nucleophilic additions to nitrones [8] or cycloadditions of nitrones with electron rich alkenes [9–11]. Only few isolated and structurally characterised complexes are described in the literature, usually with metals in fairly low oxidation states, e.g., Ru(II) or Os(II) porphyrins [12], Rh(I) carbonyl complexes [13], or M(II) coordination compounds (M = Ni, Co, Cu, Mn, Fe) [14–17]. As a rare example of a complex of a metal in high oxidation state, a Ti(IV) compound of the composition $[Cp_2Ti(\text{nitrone})_2]^{2+}$ was isolated and structurally characterised [18]. Interestingly, nitrone complexes can also be synthesised in the coordination sphere of a metal, e.g., by reaction of an iron carbene complex with nitrosobenzene [19]. In all cases, the nitrone binds to the metal via its oxygen atom, further supporting the structure proposed for the complexes described here.

4. Hydrolysis of the nitrone

When $[MoCl_4(MeCN)_2]$ or $[WCl_4(MeCN)_2]$ is reacted with 2 equivalents of a nitrone in acetonitrile as solvent, an approximate 1:1 mixture of nitrone and aldehyde is formed, suggesting that these transition metals assist in the hydrolysis of the nitrone. No evidence was found for the existence of a nitrone complex since all NMR signals of the nitrone appear at their usual positions. Also, no signals of free or coordinated oxadiazoline were detected. With this, the Mo and W complexes are clearly distinct from the analogous Pt, Ti and Zr compounds.

The difference to Ti and Zr can be rationalised in terms of complex stability. It is known that the W and Mo complexes do not dissociate, even in solvents other than the parent nitrile [20]. The Ti and Zr complexes, in contrast, are known to exist in an equilibrium between $[MCl_4(RCN)_2]$ and $[MCl_4(RCN)] + RCN$ in solution [21]. Ligand exchange is therefore more likely to occur with Ti or Zr than with Mo or W.

Free nitrones hydrolyse only slowly under both acidic and basic aqueous conditions [22]. In the reaction with Pt, Pd, Ti or Zr nitrile complexes a small amount of aldehyde is usually produced as a by-product, indicating that hydrolysis can occur as a side reaction. However, with $[MoCl_4(MeCN)_2]$ and $[WCl_4(MeCN)_2]$ hydrolysis becomes the major reaction pathway, even if the reaction is performed in dried solvents and in a nitrogen atmosphere. Coordination of the nitrone to the metal is not likely to be responsible for an activation towards hydrolysis since the release of coordinated nitrone from the Ti and Zr complexes described in the previous section occurs without concomitant hydrolysis, even upon shaking the sample with water. Additionally, some Ru(II) and Os(II) nitrone complexes described in the literature were prepared by displacement of coordinated water by nitrone [12], without hydrolysis of the nitrone. We therefore propose an alternative mechanism, in which the nitrone oxygen atom adds to the nitrile carbon to generate an intermediate 1,5-dipole. If this intermediate is trapped by water before ring closure to the oxadiazoline occurs, a α-hydroxyamine is produced which then breaks down into an aldehyde. Such mechanism is supported by our previous quantum chemical calculations [6], which showed that in presence of a Lewis acid the cycloaddition of nitrones to nitriles indeed becomes a stepwise reaction, with the O–C bond formation occurring first. Due to its polarity, the intermediate is stabilised in polar solvents (e.g., acetonitrile used in the experiment), and reaction with water might therefore successfully compete with the second step of the cycloaddition. A more detailed study to support this mechanism is underway in this group.

5. Concluding remarks

Structurally closely related transition metal nitrile complexes behave differently in the reaction with nitrones, depending on the metal. Cycloaddition across the C≡N bond takes place if the nitrile binds strongly to the metal and ligand exchange is slow. Metals from the platinum group are most promising to favour this reaction pathway. Metals with suitable exchange kinetics and weak affinity to nitriles prefer to undergo ligand exchange, and oxygen-bound nitrone complexes are obtained if oxophilic metals such as Ti or Zr are used. A third reaction mode, i.e., hydrolysis of the nitrone to the aldehyde, was observed as the main reaction with Mo and W but also occurred with other metals as a side reaction. However, the factors leading to a preference for this reaction mode, its mechanism and the role of the metal are not yet understood and subject of a continuing study in our group.

In summary, this work shows that Lewis acidity of a metal alone is not sufficient to bring about a cycloaddition of nitrones to coordinated nitriles. Factors favouring competing reactions such as ligand exchange or hydrolysis have to be considered, and therefore, the metal strongly influences the outcome of the reaction.

6. Experimental

6.1. Materials and instrumentation

Transition metal complexes and nitrones were prepared according to published methods. Solvents were dried using standard techniques, reactions with Ti, Zr, Mo and W compounds were performed in a nitrogen atmosphere. Melting points were determined in sealed tubes on a Kofler melting point apparatus. 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 matrices were obtained on a Finnigan MAT 900XLT instrument. ^{1}H and ^{13}C NMR experiments were acquired on Bruker DRX 500 and Bruker AMX 300 spectrometers at ambient temperature.

6.2. Preparation of palladium(II) oxadiazoline complexes via cycloaddition

$[PdCl_2(PhCN)_2]$ (65 mg, 0.17 mmol) was dissolved in hot (56 °C) benzonitrile (0.5 ml). Then the corresponding nitrone (0.34 mmol) was added as a solid and the reaction mixture left standing without stirring for 2 days at room temperature. The orange solid formed was filtered off, washed with diethylether, and recrystallised from CH_2Cl_2/diethylether.

$[PdCl_2\{\overline{N{=}C(Ph)O{-}N(Me){-}C}H(Ph)\}_2]$ Yield is 58%. *Anal.* Calc. for $C_{30}H_{28}Cl_2N_4O_2Pd$: C, 55.11; H, 4.32; N, 8.57. Found: C, 55.73; H, 4.29; N, 8.50%. FAB$^+$-MS, *m*/*z*: 677 [M + Na]$^+$, 617 [M– HCl]$^+$, 583 [M–2HCl]$^+$. M.p. 166 °C. IR spectrum (selected bands), cm^{-1}: 1627 vs ν(C=N) + ν(C=C). ^{1}H NMR spectrum in $CDCl_3$, δ: 2.94 (s, 3*H*, C–N(*Me*)–O), 5.89 (s, br, 1*H*, N–C*H* –N), 7.40 (t, 7.5 Hz, 2*H*), 7.50 (m, 3*H*), 7.68 (m, 3*H*), and 8.63 (d, 7.5 Hz, 2*H*) (two Ph). ^{13}C NMR spectrum in $CDCl_3$, δ : 45.8 (br, C–N(*Me*)–O), 93.7 (br, N–*C*H–N), 122.6, 128.5, 128.7, 128.9, 129.8, 130.4, 133.5 and 135.8 (two Ph), 164.9 (C=N).

$[PdCl_2\{\overline{N{=}C(Ph)O{-}N(Me){-}C}H(p\text{-}C_6H_4Me)\}_2]$ Yield is 44%. *Anal.* Calc. for $C_{32}H_{32}Cl_2N_4O_2Pd$: C, 56.36; H, 4.73; N, 8.22. Found: C, 56.48; H, 4.88; N, 8.41%. FAB$^+$-MS, *m*/*z*: 705 [M + Na]$^+$, 610 [M–2HCl]$^+$. M.p. 150 °C (dec.). IR spectrum (selected bands), cm^{-1}: 1632 vs ν(C=N) + ν(C=C). ^{1}H NMR spectrum in $CDCl_3$, δ: 2.44 (s, 3*H*, C_6H_4*Me*), 2.95 (s, 3*H*, C–N(*Me*)–O), 5.87 (s, br, 1*H*, N–C*H*–N), 7.30 (d, 7.8 Hz, 2H), 7.48 (d, 7.9 Hz, 2H)(C_6H_4Me), 7.40 (t, 7.6 Hz, 2*H*), 7.63 (m, 1*H*) and 8.68 (d, 7.6 Hz, 2*H*)(Ph). ^{13}C NMR spectrum in $CDCl_3$, δ : 21.5 (C_6H_4*Me*), 46.0 (br, C–N(*Me*)–O), 93.8 (br, N–*C*H–N), 122.5, 128.1, 128.6, 128.7, 129.1, 129.3, 130.4, 133.0, 133.5, 139.4 (Ph and C_6H_4Me), 164.3 (C=N).

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