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Platinum(IV)-Mediated Nitrile–Amidoxime Coupling Reactions: Insights into the Mechanism for the Generation of 1,2,4-Oxadiazoles

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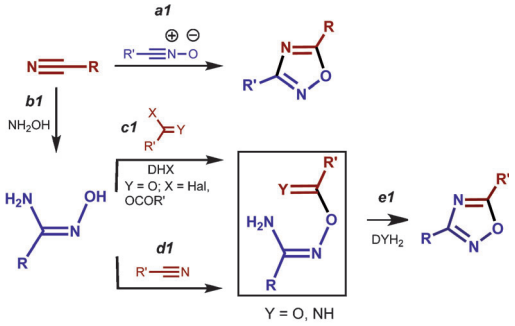
The nucleophilic addition of amidoximes R′C(NH_2)=NOH (**4**: R′ = Me, **5**: CH_2Ph, **6**: Ph) to coordinated nitriles in the platinum(IV) complexes *trans*-[$PtCl_4$(RCN)$_2$] (**1**: R = Et, **2**: Ph, **3**: NMe_2) proceeds in a 1:1 molar ratio and leads to the monoaddition products [$PtCl_4$(RCN){H*N*=C(R)ONC(R′)NH_2}] (**7**: R/R′: Et/CH_2Ph, **8**: Et/Ph, **9**: NMe_2/CH_2Ph, **10**: NMe_2/Ph). Meanwhile, if the nucleophilic addition proceeds in a 2:1 molar ratio the reaction gives the bisaddition species [$PtCl_4${H*N*=C(R)ONC(R′)NH_2}$_2$] (**11**: R/R′ = Et/Me, **12**: Et/CH_2Ph, **13**: Et/Ph, **14**: Ph/Ph, **15**: NMe_2/Me, **16**: NMe_2/CH_2Ph, **17**: NMe_2/Ph). All complexes **7**–**17** bear nitrogen-bound O-iminoacylated amidoxime groups. The addition of one equivalent of the corresponding amidoxime to each of **7**–**10** leads to **12**, **13**, **16**, and **17**, respectively. Complex [$PtCl_4$($NCNMe_2$){H*N*=C(NMe_2)ONC(Ph)NH_2}] (**10**), when dissolved in $MeNO_2$, gave *mer*-[$PtCl_3$-{H*N*=C(NMe_2)O*N*C(Ph)NHC(NMe_2)=*N*H}] (**18**) with the newly formed tridentate ligand derived from an unexpected coupling between two Me_2NCN ligands and the N and the O centers of the amidoxime. The O-imidoylamidoxime compounds R′C(NH_2)=NOCR(=NH) (**19**–**25**) were liberated from the corresponding complexes **11**–**17** by treatment with excess NaCN and these metal-free species were characterized by ^{1}H and ^{13}C{^{1}H} NMR spectroscopy. The conversion of **19**–**25** into the 3,5-substituted 1,2,4-oxadiazole compounds O^{a}N=C(R′)N=C^b(R)$^{(a–b)}$ (**26**: R/R′ = Me/Et, **27**: $PhCH_2$/Et, **28**: Ph/Et, **29**: Ph/Ph, **30**: Me/NMe_2, **31**: $PhCH_2$/NMe_2, **32**: Ph/NMe_2) occurs at room temperature and the cyclization is promoted by strong acceptor substituents R′.

Introduction

1,2,4-Oxadiazole derivatives represent an important class of five-membered heterocycles, and their versatile chemistry has been repeatedly reviewed over the years.[1] The increased number of publication about the oxadiazoles relates to the importance of these heterocycles and their derivatives in both materials chemistry (e.g. they serve as components of polymers,[1a] liquid crystals and ionic liquids,[1a,2] luminescent[1a,2c] and optoelectronic materials,[1a] and corrosion inhibitors[3]) and medicinal chemistry[1a,4] (e.g. they are applied as antidiabetic,[1a] antiinflammatory,[1a,5] antimicrobial,[1a,2a,6] antitumor agents,[1a,4,7] immunosuppressors,[1a,2a] and neuroprotective agents,[1a,2a,4,8] as well as compounds exhibiting fungicidal and larvicidal properties[9]). Among the known synthetic strategies for the generation of 1,2,4-oxadiazoles, the two most common approaches include the 1,3-dipolar cycloaddition of nitrile oxides to nitriles (Scheme 1 path *a1*) and the reaction of amidoximes with activated carboxylic acids and a wide variety of their derivatives (path *c1* and *e1*) or nitriles (path *d1* and *e1*).[1a] The boxed intermediate with Y = NH shown in Scheme 1 has never been observed in the past, although it is known for Y = O.

The syntheses of 1,2,4-oxadiazoles that are based on the reaction between RCN and amidoximes species[10] require rather harsh conditions (100–180 °C) when performed with metal-free protocols.[11] Alternatively, these reactions could be conducted as metal-mediated processes under milder conditions (20–80 °C)[10a,c,d] in the presence of catalytic amounts of $ZnCl_2$ (and subsequent addition of HCl[10d] or *p*-toluenesulfonic acid, PTSA[10a]). Many more reactive substrates bearing the C≡N group (e.g. nitrilium salts) were also transformed into 1,2,4-oxa-



Scheme 1. Synthetic strategies for the generation of 1,2,4-oxadiazole derivatives.

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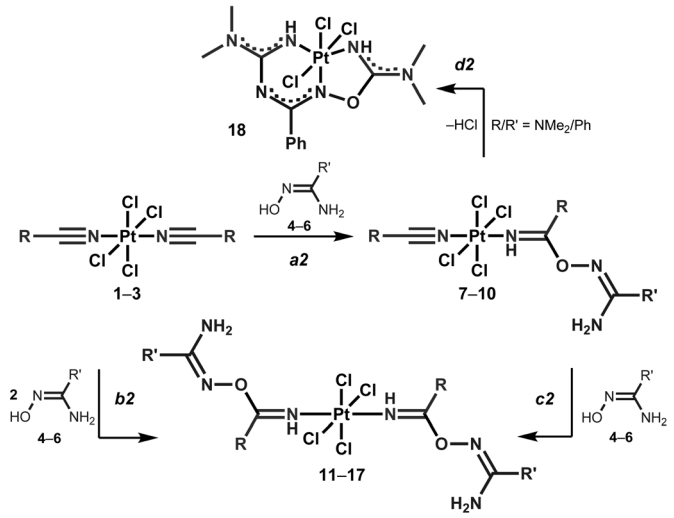
diazoles upon their reaction with amidoximes, and this process occurs through the cyclization of the initially formed iminium salt.[10b]

Our research group has been interested in extending our ongoing project on nucleophilic additions to the metal-activated CN triple bond (for reviews see reference [12], for recent studies see reference [13]), and we focused our attention on reactions of nucleophiles bearing the $(NH_2)C{=}NOH$ functionality[14] that lead to metal-stabilized O-iminoacylated amidoximes. These $HN{=}C(R)ON{=}(NH_2)CR'$ species have a similar structural unit to the proposed intermediate (Scheme 1, Y = NH) in the reaction between amidoximes and nitriles leading to 1,2,4-oxadiazoles. Our particular interest in studying the addition of the amidoximes $R'C(NH_2){=}NOH$ (R' = Me, $PhCH_2$, Ph) to the nitrile ligands in the platinum(IV) complexes *trans*-$[PtCl_4(RCN)_2]$ (R = Et, Ph, NMe_2) was at least two-fold. First, we intended the extension of the metal-mediated nitrile–oxime coupling reaction[15] to nitriles and amidoximes of various structures. Second, we anticipated the liberation of the iminoacylated amidoximes from the Pt^{IV} center for verifying a possibility for the cyclization of these metal-free species into 1,2,4-oxadiazoles. The latter experiment was planned to gain an insight into the mechanism for both the metal-free and the metal-mediated generation of 1,2,4-oxadiazoles from RCN and amidoximes.



Compds	R
1	Et
2	NMe_2
3	Ph
Compds	**R'**
4	Ph
5	CH_2Ph
6	Me

Compds	R	R'	Yield [%]
7	Et	CH_2Ph	81
8	Et	Ph	95
9	NMe_2	CH_2Ph	100 (NMR)
10	NMe_2	Ph	85
11	Et	Me	81
12	Et	CH_2Ph	91
13	Et	Ph	84
14	Ph	Ph	72
15	NMe_2	Me	79
16	NMe_2	CH_2Ph	80
17	NMe_2	Ph	85

Scheme 2. Synthetic transformations. Compound numbering and yields are given in the tables.

Results and Discussion

Iminoacylation of oximes proceeds rapidly under mild conditions when metal centers in high oxidation states (e.g. Pt^{IV}, Rh^{III}, or Re^{IV}) are applied for activation of RCN species.[15c,d,16] Therefore, as the starting materials for this study we addressed the nitrile platinum(IV) complexes *trans*-$[PtCl_4(RCN)_2]$ (R = Et, Ph, NMe_2). The reaction between the amidoximes $R'C(NH_2){=}NOH$ (**4**–**6**) and the *trans*-$[PtCl_4(RCN)_2]$ complexes (**1**–**3**) proceeded rapidly (1–10 min) at room temperature at both 1:1 and 2:1 molar ratio of the reactants and afford complexes **7**–**17** (Scheme 2, path *a2*–*c2*). Compounds **1** and **2** were treated with one equivalent of amidoximes **4** or **5** (in all possible combinations) to form monoaddition species **7**–**10** (Scheme 2, path *a2*) in 81–95% yield after column chromatography; complex **9** was not separated from some by-products (because of its close retention indexes to these species) and therefore it was characterized in the reaction mixture.

The compounds $[PtCl_4(RCN)\{HN{=}C(R)ONC(Me)NH_2\}]$ (R = Et, NMe_2)—derived from the reaction of **1** or **2** and one equivalent of **6**—decompose on silica gel and thus they were not purified by column chromatography. However, the formation of these complexes was confirmed by high resolution electrospray mass spectrometry (for R = Et: calcd for $([M-Cl]^+)$: 484.004; found: 484.011, calcd for $([M-EtCN+H]^+)$: 466.935; found: 466.943, for R = NMe_2: calcd for $([M-Cl]^+)$: 514.026; found: 514.032).

The monoaddition products formed in the reaction of *trans*-$[PtCl_4(PhCN)_2]$ (**3**) and amidoximes **4**–**6** were not be obtained because of a poor solubility of the starting complex in the most common organic solvents. Thus, for example slow addition (over 6 h) of a nitromethane solution of **4** to a vigorously stirred suspension of **3** in $MeNO_2$ in a 1:1 molar ratio of the reactants brings about a mixture of bisaddition product **14** and **3** in an approximate 1:1 ratio.

Complexes **7**–**10** were converted into corresponding bisaddition species **12**, **13**, **16**, and **17** by the reaction using than more one equivalent of the corresponding amidoxime (Scheme 2, path *c2*). Alternatively, **11**–**17** were obtained by the reaction of starting nitrile complexes **1**–**3** using two equivalents of amidoximes **4**–**6** (in all possible combinations) in a CH_2Cl_2 solution for 1–10 minutes at room temperature (72–91%; Scheme 2, path *b2*). Reaction between benzonitrile complex **3** and each of the aliphatic amidoximes (**5** and **6**) upon vigorous stirring in the commonly used organic solvents (CH_2Cl_2, $CHCl_3$, Me_2CO, MeOH, and EtOH) accompanied by ultrasound treatment of suspensions led to a mixture of yet unidentified products where uncomplexed benzonitrile was detected, but no amidoxime addition products were observed in ESI-MS.

As far as the driving forces of the coupling is concerned, no reaction between each of **4**–**6** and benzonitrile, propiononitrile, or dimethylcyanamide in either CD_2Cl_2 or $[D_6]Me_2SO$ was observed for seven days at room temperature. These blank experiments suggest that the nucleophilic addition of the amidoximes to the RCN species is mediated by Pt^{IV}.

Before the above-described experiments, only one example of the nitrile–amidoxime coupling reaction had been report-

ed.[14] It was observed that the heterogeneous reaction between $[PtCl_4(MeCN)_2]$ and the amidoxime $PhC(NH_2)=NOH$ requires prolonged heating (27 h at 56 °C) owing to poor solubility of the starting platinum(IV) material. We found that in the homogenous liquid media the nitrile–amidoxime coupling proceeded even faster than the previously described[15d] nitrile–ketoxime coupling (1–10 min at 20–25 °C vs. 10 min at 55–60 °C, respectively) and this phenomenon can be explained by the $+M$ effect of the NH_2 group[17] that increases the nucleophilicity of the oxime functionality.

Characterization of complexes 7–17

Complexes **7**–**17** give satisfactory C, H, and N elemental analyses for the proposed formulae (**10** was characterized only in situ) and these species were also characterized by IR, high resolution ESI-MS, and NMR spectroscopy techniques; the structures of seven complexes (**8**, **11**, and **13**–**17**) were studied by X-ray crystallography. Complexes **11**, **13**, and **17** crystallized as the Me_2CO solvates, whereas **16** and **17** formed solvates **16**·$^1/_2H_2O$ and **17**·$2CHCl_3$; no solvent was observed in the crystal lattices of **8**, **14**, and **15** (Figure 1, Figure 2, Figure 3, and Figures **S1**–**S5** in the Supporting Information).

The imino ligands in **7**–**17** exist in the different *E* (R = Et, Ph; for **7**, **8**, **11**–**14**) or *Z* (R = NR'_2; for **9**, **10**, **15**–**17**) forms as confirmed by IR and NMR data, and

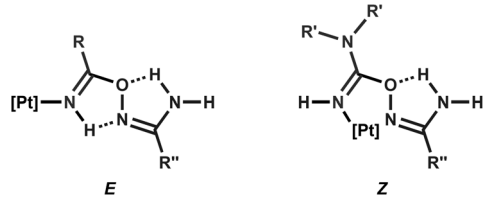


Figure 1. *E* configuration (left; for **7**, **8**, **11**–**14**) and *Z* configuration (right; for **9**, **10**, **15**–**17**) of the iminoacylated amidoxime ligands.

also by X-ray crystallography (see Figure 1 and see the Supporting Information for detailed discussion of the NMR and X-ray data). The difference in the *E* and *Z* configurations for **7**–**17** could be accounted for by a fine balance between steric factors and degree of conjugation of the substituents R or NR'_2 with the platinum(IV)-bound imino group.

Unexpected nitrile–amide coupling

We observed that **10**, being dissolved in $MeNO_2$, underwent gradual conversion at room temperature for three weeks and gave a mixture of metal-containing species. When the solvent was evaporated at 20–25 °C to dryness, the brownish oily residue that was formed contained a small amount of red crystals that were mechanically separated and studied by X-ray crystallography (Figure 4). The obtained X-ray data disclose the structure of **18** that, at least formally, originates from an unusual coupling between two Me_2NCN ligands and the N and O centers of the oxime (Scheme 2, path *d2*).

All attempts to optimize reaction conditions to increase yield of **18**, such as alteration of the solvent ($CHCl_3$, Me_2CO, MeOH, EtOH, and $MeNO_2$ were tested), varying temperature in

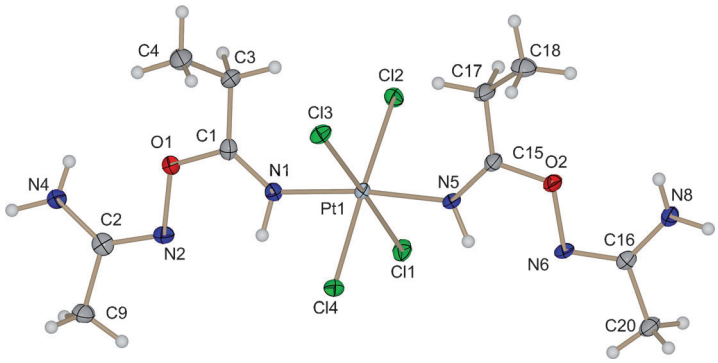


Figure 2. ORTEP structure of **11** with the atom-numbering scheme. Thermal ellipsoids are drawn at the 50% probability level. The imino ligands adopt the *E* configuration.

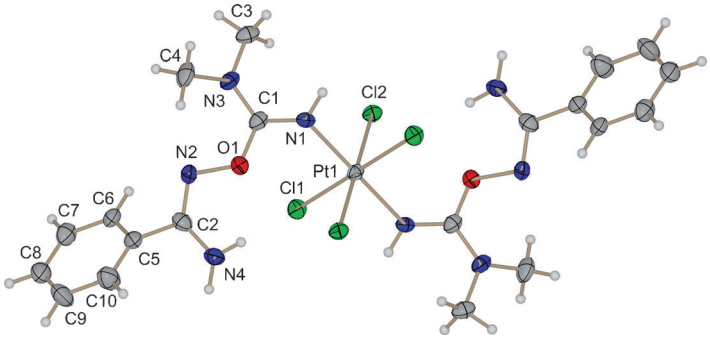


Figure 3. ORTEP structure of **17** with the atom-numbering scheme. Thermal ellipsoids are drawn at the 50% probability level. The imino ligands adopt the *Z* configuration.

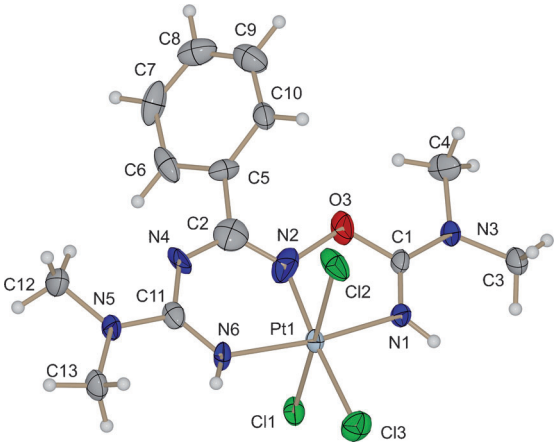


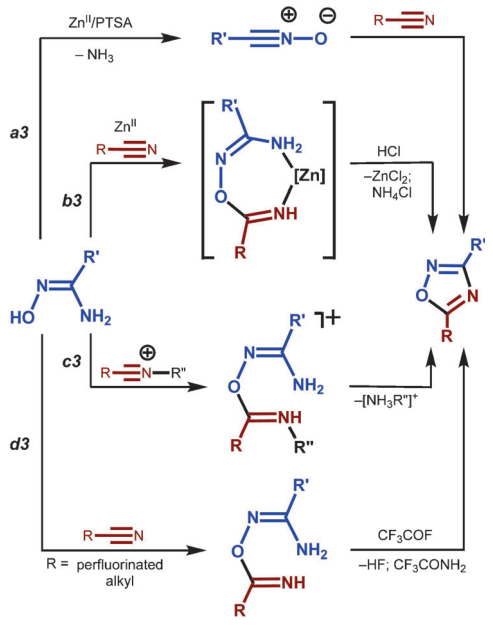
Figure 4. ORTEP structure of **18** with the atom-numbering scheme. Thermal ellipsoids are drawn at the 50% probability level. Selected bond lengths [Å] and angles [°]: Pt1–N2 1.959(5), Pt1–N1 2.000(4), Pt1–N6 2.012(4), N1–C1 1.292(6), N3–C1 1.324(7), N2–C2 1.257(7); N2-Pt1-N1 80.2(2), N2-Pt1-N6 91.5(2), N1-Pt1-N6 171.70(17).

the range from 20 to 100 °C (depending on b.p. of the employed solvent), additions of a base to deprotonate the amide moiety (stoichiometric quantities of pyridine or solid $NaHCO_3$ were added), or addition of one equivalent $AgSO_3CF_3$ to abstract a chloride atom and to promote the coupling, were so far unsuccessful. In spite of that, we believe that our observations deserve further investigation of other similar systems insofar as the coupling is a rare example of nitrile–amide coupling[18] and the first example of the dual reactivity of amidoximes toward nitriles. In addition, the NCNCN[Pt] ring is relevant to 1,3,5-triazapentadiene chelates,[19] with respect to a class of complexes intensively studied in the past five years.[20]

Insight into the mechanism for the generation of 1,2,4-oxadiazoles from nitriles and amidoximes

Among purely synthetic studies, some works dealt with the mechanism for the generation of 1,2,4-oxadiazole derivatives in the reaction between nitrile and amidoxime functionalities[10] and these reports illustrate different views on occurrence of the reaction (Scheme 3).

Augustine et al.[10a] applied the $ZnCl_2$/PTSA system to facilitate the nitrile–amidoxime interaction and assumed that the zinc(II) center abstracts ammonia from the amidoxime to give the nitrile oxide, which then reacts with the nitrile group as a 1,3-dipole (Scheme 3, path *a3*). Yarovenko et al.[10d] employed the ^{15}N NMR technique to study the mechanism for the generation of the oxadiazoles in the reaction between nitriles and amidoximes catalyzed by the $ZnCl_2$/HCl system and suggested, albeit intermediates were not separated individually, that the nitrile–amidoxime integration proceeds in the coordination sphere of Zn^{II} followed by formation of a bidentate coordinated imine (Scheme 3, path *b3*). Hydrochloric acid, which is added after the zinc salt, is required for decoordination of the



Scheme 3. Previously suggested mechanisms for the generation of 1,2,4-oxadiazole derivatives from nitrile and amidoxime functionalities.

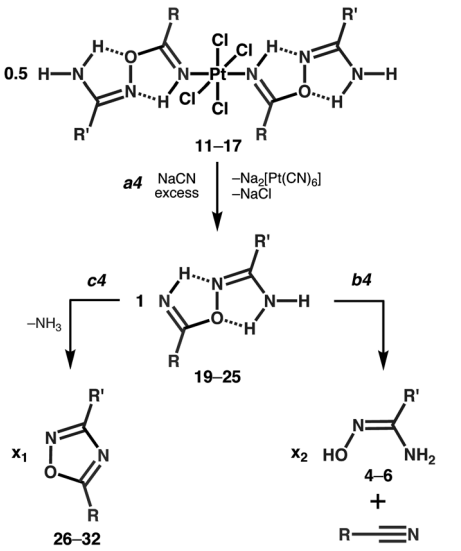
imine. The latter, after the liberation of the HN= functionality, give the oxadiazole via cyclization. Yet another report[10b] describes a facile nitrilium salt/amidoxime interplay leading to the moderately stable iminium salts, which then under heating undergo cyclization to achieve the 1,2,4-oxadiazoles (Scheme 3, path *c3*). Kabakchi et al.[21] synthesized O-imidoylamidoximes starting from nitriles bearing strong acceptor perflourinated alkyl groups as substituents. For these products no structural transformations were detected at room temperature, but addition of CF_3COF promoted the cyclization of the imines into the corresponding 1,2,4-oxadiazoles[21] (Scheme 3, path *d3*).

The Pt^{IV}-mediated reaction between the nitrile ligands and the amidoxime derivatives allows the generation of the monodentate coordinated imines HN=C(R)ON=C(NH_2)R′ under mild reaction conditions. The imino species formed are stabilized through binding to the platinum center,[22] and to study reactivity of the imines toward cyclization they should be decoordinated. For the liberation of the imino ligands we attempted different routes that are described in the paragraphs that follow.

Despite significant kinetic inertness of platinum(IV) complexes, several methods for displacement of the strongly bound open-chain imines[15b,23] and heterocycles with the –N=C– moiety[24] from their Pt^{IV} complexes have been developed and they are based on reactions with an excess amount of pyridine[23b,24] or diphosphines.[15b,23a] We observed that in **7**–**17** the newly formed imino ligands are so strongly bound to the platinum(IV) center that the decoordination cannot be achieved even in neat pyridine at 85 °C for one day. However, it was previously reported that the alkali metal cyanides could be used for decoordination of some chelated phosphine ligands[25] and N-heterocyclic ligands strongly bound to Pt^{II} centers.[13b,c] In addition, cyanides are transparent in the ^1H NMR region and this facilitates monitoring the reaction by using NMR spectroscopy. In accord with this method, imines **19**–**25** were liberated from **11**–**17**, correspondingly, by treatment with excess NaCN in a solution of $[D_6]Me_2SO$ at room temperature to furnish uncomplexed substituted *N*′-(1-iminopropoxy)imidamides (**19**–**21**), *N*′-(imino(phenyl)methoxy)benzimidamide (**22**), *N*′-((*N*,*N*-dimethylcarbamimidoyl)oxy)imidamides (**23**–**25**), and $Na_2[Pt(CN)_6]$.[13b,25]

Monitoring with ^1H and $^{13}C\{^1H\}$ NMR techniques indicates that **19**–**22**, after the liberation, undergo further conversion by two routes to give, first, the parent nitrile and amidoxime in the retrocoupling (Scheme 4, path *b4*) and, second, to produce 3,5-substituted 1,2,4-oxadiazoles (Scheme 4, path *c4*). Generation of these heterocycles was confirmed by comparison of their NMR characteristics with those for the corresponding oxadiazoles obtained by independent syntheses.[26]

We also observed that acetic acid (2 mol% with respect to **19**–**21**), which was added immediately after the liberation, has no effect on the transformation of *N*′-(1-iminopropoxy)imidamides. Meanwhile a stoichiometric quantity of the stronger picric acid (1:1 mol/mol with respect to **19**) substantially accelerates the conversions of the imine but makes the transformations less selective. Furthermore, the addition of the anhydrous



Compds	R	R'	x_1	x_2
19	Et	Me	0.12	0.88
20	Et	CH_2Ph	0.23	0.77
21	Et	Ph	0.32	0.68
22	Ph	Ph	0.19	0.81
23	NMe_2	Me	<0.03	≈0.04
24	NMe_2	CH_2Ph	<0.03	≈0.04
25	NMe_2	Ph	<0.03	≈0.04

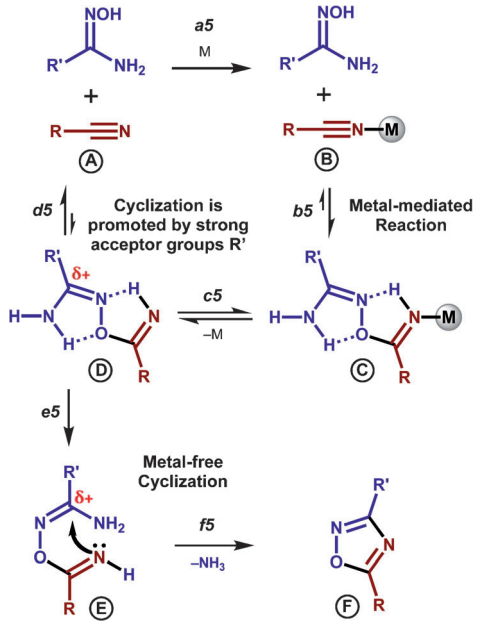
Scheme 4. Liberation of the O-iminoacylated amidoximes and their further transformations. Compound numbering and relative amount of the products are given in the table.

$ZnCl_2$ (1 mol% with respect to **19**) switches the process to the almost quantitative splitting of **19** to the parent nitrile and the amidoxime (Scheme 4, path *b4*).

^{1}H NMR data indicate that **23**–**25**, after the liberation, undergo decomposition with a half-decay period of approximately 7 minutes to yield a broad mixture of products, where, in particular, the corresponding amidoxime, dimethylcyanamide, and 3-substituted 5-dimethylamino-1,2,4-oxadiazole were detected in trace amounts, along with *N*,*N*-dimethylurea (35%, 32%, and 30%, respectively, with respect to the starting quantity of **23**–**25**).

Based upon experimental data we found that, first, the O-iminoacylated amidoxime derivatives bearing donor and moderate acceptor substituents R (R = Et, Ph, NMe_2) split to give the parent nitriles and amidoximes much faster than the imines with the strong acceptor substituents (R = perfluorinated alkyl), that is, if the former split at room temperature and the latter convert only in toluene at reflux at about 110 °C[21] (Scheme 5, path *d5* and path *e5*). Second, the cyclization of O-iminoacylated amidoximes into 3,5-substituted 1,2,4-oxadiazoles is more efficient when R′ is an acceptor group; the stronger acceptor group R′ leads to the higher yield of the heterocycles. Third, the cyclization (Scheme 5, path *e5* and path *f5*) is not affected by zinc(II). All these observations give novel insights into a plausible mechanism for the generation of 1,2,4-oxadiazoles from nitriles and amidoximes.

By summarizing the thus-far obtained experimental and the literature data, we anticipate that the reaction between nitriles



Scheme 5. Plausible mechanism for the generation of 1,2,4-oxadiazole derivatives from nitrile and amidoxime species.

and amidoximes comprises two steps. The first includes a reversible nucleophilic addition of an amidoxime to a nitrile producing an equilibrium concentration of **D** (for the metal-free process) or **C** (for the metal-catalyzed transformation; Scheme 5). The concentration of **D** is very small when R is a donor group, but becomes much higher for electron-deficient nitriles, for example, those with perfluorinated alkyl groups.[21] Furthermore, one should mentioning that metal-free intermediates structurally relevant to **D** were previously isolated as the alkylated iminium salts $[H(R'')N{=}C(R)ON{=}C(NH_2)R']^+$[10b] or as the imines $HN{=}C(R_F)ON{=}C(NH_2)R'$[21] in the reaction between the corresponding nitrilium salts or perflourinated nitriles, respectively, and amidoximes.

For path *b5* of Scheme 5 the equilibrium point strongly depends on the nature of the metal centers, that is, the equilibrium is almost completely shifted to **C** in the case of platinum(IV), while for the Zn^{II} center the concentration of the reactants is higher. However, the Zn^{II} center still activates the CN triple bond toward the nucleophilic addition to provide more iminoacylated product **C** (Scheme 5, path *b5*) than in the metal-free reaction (Scheme 5, path *d5*). In addition, the equilibrium shown in path *c5* of Scheme 5 is shifted to the right for the kinetically inert platinum(IV) center, meanwhile the kinetically labile zinc(II) center provides **D**. One should notice that the zinc(II) center more likely forms the intermediate with an open-chain rather than the chelated (see Scheme 3, path *b3*) O-iminoacylated product as suggested by Yarovenko et al.[10d] Indeed, graphical search of *Chemical Abstracts* gives 23 structures where amidoximes behave as bidentate ligands with the five-membered amidato ring M{*O*-N=C(*R*)-*N*H} and no structures similar to that shown in Scheme 3 were found.

In the second step, **D** undergoes an intramolecular cyclization (Scheme 5, path *e5* and path *f5*) to form 3,5-substituted 1,2,4-oxadiazole **F**. This reaction does not require a metal

center, however, the cyclization is more efficient when **D** bears strong acceptor groups R′; the latter functionalities facilitate intramolecular nucleophilic attack (**E**). Ammonia (Scheme 5, path *f5*) derives from the R′CNH_2 moiety as confirmed by the ^{15}N NMR study.[10d]

Conclusion

In the area of coordination chemistry, we observed the stepwise coupling between nitriles and amidoximes that is mediated by the platinum(IV) center (Scheme 2) and proceeds faster than the relevant couplings involving ketoximes. The *E/Z* configuration of the formed iminoacylated amidoxime ligands depends on the R substituent in the starting RCN ligands—the ligand is *E* configured for R = Et or Ph and always *Z* configured for the dialkylcyanamide (Figure 1–Figure 3). Furthermore, by identification of tridentate product **18** (Scheme 2 and Figure 4), we found a rare example of nitrile–amide coupling[18] and the first example of the dual reactivity of amidoximes toward nitriles.

All open-chain iminoacylated ligands formed in the coupling reaction were liberated by the reaction of the platinum(IV) complexes with NaCN (Scheme 4). As a consequence, in the area of metal-free organic chemistry, we observed rather fast transformation of the O-iminoacylated amidoxime species by two routes to achieve either parent nitriles and amidoximes (formed through retrocoupling) or 1,2,4-oxadiazoles (generated by intramolecular cyclization). These experiments give novel insights into a plausible mechanism for the generation of 1,2,4-oxadizoles upon the reaction between nitriles and amidoximes, and suggests that it involves the nucleophilic attack of amidoximes to the nitrile group followed by the cyclization of thus formed O-iminoacylated oxime; if the former step is affected by a metal center, the latter proceeds as a metal-free process (Scheme 5).

Experimental Section

Materials and instrumentation

Solvents were obtained from commercial sources and used as received. The amidoximes were synthesized by literature methods.[27] Complexes *cis/trans*-$[PtCl_2(RCN)_2]$ (R = Et[28], Ph[29], NMe_2[30]) were synthesized in accord with the published procedures;[28–30] the *cis*- and *trans*-isomers were separated by column chromatography on silica gel (SiO_2 60 F_{254}, 0.063–0.200 mm, Merck). The platinum(IV) complexes *trans*-$[PtCl_4(RCN)_2]$ were obtained by chlorination of the corresponding platinum(II) species.[15d,30,31] TLC was performed on Silufol UV254 SiO_2 plates. Elemental analyses for C, H, and N were carried out on a Hewlett Packard 185 B Carbon Hydrogen Nitrogen Analyzer. The electrospray ionization mass spectra were measured on a Bruker micrOTOF spectrometer equipped with electrospray ionization (ESI) source. The instrument was operated both in positive and negative ion mode using an *m/z* range of 50–3000. The capillary voltage of the ion source was set at −4500 V (ESI-MS) and the capillary exit at ±(70–150) V. The nebulizer gas flow was 0.4 bar and drying gas flow was 4.0 L min^{-1}. For ESI analysis the compounds were dissolved in MeOH or MeCN. In the isotopic pattern, the most intensive peak is reported. The infrared spectra (4000–400 cm^{-1}) were recorded on a Shimadzu FTIR-8400S instrument in KBr pellets. The ^1H and $^{13}C\{^1H\}$ NMR spectra were measured on a Bruker DPX 300 spectrometer at ambient temperature in $[D_6]Me_2CO$, $[D_6]Me_2SO$, or $CDCl_3$; residual solvent signals were used as internal standards.

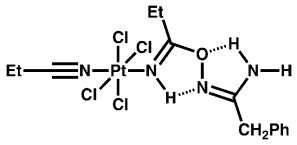
X-ray crystal structure analysis

The crystals of **8**, **11**, and **13–18** were immersed in cryo-oil, mounted in a Nylon loop, and measured at a temperature of 100 K. The X-ray diffraction data were collected on a Bruker Axs Smart Apex II, Bruker Axs Kappa Apex II, or Nonius KappaCCD diffractometer using Mo Kα radiation (λ = 0.71073 Å). The Apex2[32] or Denzo-Scalepack[33] program packages were used for cell refinements and data reductions. The structures were solved by direct methods using the SIR97,[34] SIR2008,[35] SUPERFLIP,[36] or SHELXS-97[37] program with the WinGX[38] graphical user interface. A semiempirical or numerical absorption correction (SADABS[39]) was applied to all data. Structural refinements were carried out using SHELXL-97.[37] In **11**, the acetone of crystallization was disordered over two sites around a center of symmetry with equal occupancy. The heavy atoms of the disordered molecule were restrained so that their U_{ij} components approximate to isotropic behavior. These atoms were further constrained so that they all have equal displacement parameters. In **14**, one of the phenyl rings (C9–C14) was disordered over two sites with equal occupancies. In these rings, the carbon atoms C9, C10, C9B, and C10B were restrained so that theirs U_{ij} components approximate to isotropic behavior. In **8**, **11**, **16**, **17**, and **18**, the hydrogen atoms of NH, NH_2 and H_2O were located from the difference Fourier map but constrained to ride on their parent atom, with U_{iso} = 1.5 U_{eq}(parent atom). In **13**, the hydrogen atoms of NH and NH_2 were located from the difference Fourier map and refined isotropically. All other hydrogen atoms were positioned geometrically and constrained to ride on their parent atoms, with C–H = 0.95–0.99 Å, N–H = 0.88 Å, and U_{iso} = 1.2–1.5 U_{eq}(parent atom). The crystallographic details are summarized in Table S2 in the Supporting Information.

Synthesis

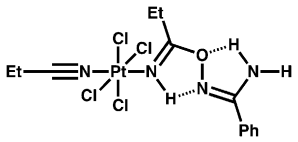
General method for the nucleophilic addition of amidoximes to the (nitrile)Pt^{IV} complexes

Nucleophilic addition of R′$C(NH_2)$=NOH (1 equiv) to *trans*-$[PtCl_4(RCN)_2]$ (R = NMe_2; Et): A solution of amidoxime (0.075 mmol) in dichloromethane (2 mL) was added dropwise to an vigorously stirred solution of *trans*-$[PtCl_4(RCN)_2]$ (R = NMe_2; Et; 0.075 mmol) in dichloromethane (25 mL, R = Et; 10 mL, R = NMe_2) over 15 min at RT. After stirring for 5 min at RT the resulting solution was subjected to column chromatography on silica gel (eluent: acetone/chloroform = 1:10, 0.2:2.0 mL). The first fraction was collected and the solvent was evaporated under vacuum at 20–25 °C. The resultant crystalline residues were dried in air at RT.

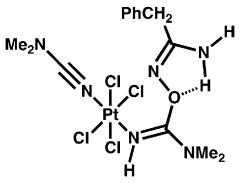


Compound **7**: Yield 81 %. m.p. 133 °C (decomp); ^1H NMR (300 MHz, $CDCl_3$, 20 °C): δ = 8.78 (s, br, 1 H, NH), 7.45–7.25 (m, 5 H, Ph), 4.86 (s, br, 2 H, NH_2), 3.26 (q, 2 H, CH_2), 3.10 (q, 2 H, CH_2), 1.53 (t, 3 H, CH_3),

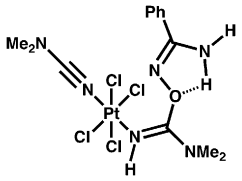
1.31 ppm (t, 3H, CH_3); the signals of Et_2O (1.20, t and 3.48 ppm, q) were detected in the spectrum, their integral intensities are in agreement with the elemental analyses data; IR (KBr, selected bonds): $\nu(N_{amide}–H) = 3476$ (m-s), 3352 (s); $\nu(N_{imine}–H\cdots N) = 3253$ (m, br); $\nu(C–H) = 3059$ (w), 3029 (w), 2987 (w-m), 2941 (w), 2921 (w), 2881 (w); $\nu(C{\equiv}N) = 2340$ (m-s); $\nu(C{=}N)_{oxime}$ and/or $\nu(C{=}N)_{imine} = 1653$ (m); $\nu(C{=}N)_{imine}$ and/or $\nu(C{=}N)_{oxime}$ and $\delta(N–H) = 1627$ (vs, br); $\delta(C–H) = 1492$ (m), 1464 (s), 1438 (s); $\delta(N_{amide}–H) = 1406$ (m-s); $\delta(C–H)_{Ar} = 722$ (m), 703 (m); $\delta(C–H) = 627$ (w), 544 (m) cm^{-1}; HRESI-MS: *m/z* calcd for $([2M–EtCN+H]^+)$: 1139.963; found: 1139.991; calcd for $([2M–EtCN+Na]^+)$: 1161.945); found: 1161.939; elemental analysis (%) calcd for $C_{14}H_{20}N_4Cl_4OPt\cdot{}^1/_4Et_2O$: C 29.26, H 3.68, N 9.10; found: C 29.18, H 3.55, N 9.22; TLC (eluent: chloroform/acetone = 5:1, 2:0.4 mL) $R_f = 0.65$.



Compound **8**: Yield 95%. m.p. 144 °C (decomp); ^1H NMR (300 MHz, $CDCl_3$, 20 °C): $\delta = 8.87$ (s, br, 1H, NH), 7.66 (d, 2H, *o*-CH), 7.58 (t, 1H, *p*-CH), 7.49 (t, 2H, *m*-CH), 5.32 (s, br, 2H, NH_2), 3.32 (q, 2H, CH_2), 3.10 (q, 2H, CH_2), 1.52 (t, 3H, CH_3), 1.39 ppm (t, 3H, CH_3); the signals of Et_2O (1.20, t and 3.48 ppm, q) were detected in the spectrum, their integral intensities are in agreement with the elemental analyses data; IR (KBr, selected bonds): $\nu(N_{amide}–H) = 3548$ (w), 3482 (m), 3415 (m), 3362 (m); $\nu(N_{imine}–H\cdots N) = 3245$ (w-m, br); $\nu(C_{Ar}–H) = 3067$ (vw); $\nu(C–H)(CH_2) = 2984$ (w), 2917 (w) $\nu(C–H)(CH_3)$; 2942 (w), 2852 (w); $\nu(C{\equiv}N) = 2327$ (w-m); $\nu(C{=}N)_{oxime}$ and/or $\nu(C{=}N)_{imine} = 1663$ (m); $\nu(C{=}N)_{imine}$ and/or $\nu(C{=}N)_{oxime}$ and $\nu(C{=}C)_{Ar}$ and $\delta(N–H) = 1617$ (vs, br); $\nu(C{=}C)_{Ar} = 1565$ (m); $\nu(C{=}C)_{Ar}$ and $\delta(C–H)_{Et} = 1466$ (m), 1430 (m); $\delta(N_{amide}–H) = 1406$ (m); $\delta(C–H)_{Ar} = 775$ (m), 697 (m-s); $\delta(C–H)_{Et} = 634$ (w-m) cm^{-1}; HRESI-MS: *m/z* calcd for $([M–Cl]^+)$: 547.014; found: 547.011; calcd for $([2M–H+Na]^+)$: 1187.948; found: 1187.965; elemental analysis (%) calcd for $C_{13}H_{18}N_4Cl_4OPt\cdot Et_2O$: C 27.71, H 3.37, N 9.37; found: C 27.59, H 3.11, N 9.42; TLC (eluent: chloroform/acetone = 5:1, 2:0.4 mL) $R_f = 0.70$; crystals suitable for X-ray diffraction were grown by the slow evaporation in air at RT of a solution in acetone/chloroform.

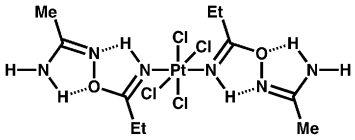


Compound **9**: 100% yield based on ^1H NMR data. ^1H NMR (300 MHz, $CDCl_3$, 20 °C): $\delta = 7.35–7.28$ (m, 5H, Ph), 5.99 (s, br, 1H, NH), 5.56 (s, br, 1H, NH), 4.84 (s + d, $^2J_{H,Pt} = 34$ Hz, br, 1H, NH), 3.18 (s, 6H, NMe_2), 3.15 (s, 2H, CH_2), 3.11 ppm (s, 6H, NMe_2); IR (KBr, selected bonds): $\nu(N_{amide}–H) = 3473$ (s), 3415 (s); $\nu(N_{imine}–H) = 3336$ (m); $\nu(C–H) = 2969$ (w), 2932 (w), 2851 (w), 2828 (w); $\nu(C{\equiv}N) = 2305$ (m); $\nu(C{=}N)$ and/or $\nu(C{=}C) = 1653$ (m-s), 1637 (s), 1617 (s); $\delta(C–H) = 775$ (w), 704 (w) cm^{-1}; HRESI-MS: *m/z* calcd for $([M–NCNMe_2+Na]^+)$: 579.959; found: 579.948; calcd for $([M–Cl]^+)$: 590.057; found: 590.050; calcd for $([2M–Cl]^+)$: 1216.078; found: 1216.067; TLC (eluent: chloroform/acetone = 10:1, 2:0.2 mL) $R_f = 0.43$.

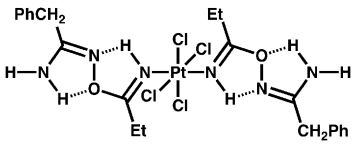


Compound **10**: Yield 85%. m.p. 139 °C (decomp); ^1H NMR (300 MHz, $CDCl_3$, 20 °C): $\delta = 7.65$ (d, 2H, *o*-CH), 7.53–7.39 (2 t, 3H, *m*-CH and *p*-CH), 5.79 (s, br, 2H, NH_2), 4.88 (s + d, $^2J_{H,Pt} = 34$ Hz, br, 1H, NH), 3.21 (s, 6H, NMe_2), 3.13 ppm (s, 6H, NMe_2); IR (KBr, selected bonds): $\nu(N_{amide}–H) = 3466$ (m), 3384 (m); $\nu(N_{imine}–H) = 3362$ (m); $\nu(C{\equiv}N) = 3052$ (w), 2934 (w) $\nu(C–H)$; 2307 (m); $\nu(C{=}N)$ and/or $\nu(C{=}C) = 1648$ (m), 1621 (s); $\delta(N–H)$ and/or $\nu(C{=}N)$ and/or $\nu(C{=}C) = 1577$ (w); $\delta(C–H) = 773$ (w), 703 (w) cm^{-1}; HRESI-MS: *m/z* calcd for $([M–NCNMe_2+Na]^+)$:564.941; found: 564.930; calcd for $([M–Cl]^+)$: 577.036; found: 577.029; calcd for $([M–Cl–H+Na]^+)$: 599.018; found: 599.011; calcd for $([M–Cl–H+K]^+)$: 614.992; found: 614.986; calcd for $([2M–Cl]^+)$: 1191.041; found: 1191.010; calcd for $([3M–2Cl–H]^+)$: 1767.069; found: 1767.026; elemental analysis (%) calcd for $C_{13}H_{20}N_6Cl_4OPt$: C 25.46, H 3.29, N 13.70; found: C 25.78, H 3.19, N 13.29; TLC (eluent chloroform/acetone = 5:1, 2:0.4 mL) $R_f = 0.52$.

Nucleophilic addition of $R'C(NH_2){=}NOH$ (2 equiv) to *trans*-$[PtCl_4(RCN)_2]$: A solution of $R'C(NH_2){=}NOH$ ($R' = Ph$, CH_2Ph, Me; 0.15 mmol) in dichloromethane (1 mL) or in nitromethane (2 mL, R = Ph) was added to a homogeneous solution of *trans*-$[PtCl_4(RCN)_2]$ ($R = NMe_2$, Et; 0.075 mmol) in dichloromethane (20 mL, R = Et; 10 mL, $R = NMe_2$) or to a suspension in nitromethane (5 mL, R = Ph) under ultrasound treatment, and stirred for 1 min (or for 10 min under ultrasound treatment, R = Ph), whereupon the solvent was evaporated to dryness at RT. The precipitates formed were washed with two portions of $CHCl_3$ (1 mL) and three portions of Et_2O (3 mL) and dried in air at 20–25 °C.

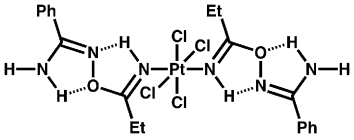


Compound **11**: Yield 81%; m.p. 154 °C (decomp); ^1H NMR (300 MHz, $[D_6]$acetone, 20 °C): $\delta = 8.74$ (s, br, 1H, NH), 6.60 (s, br, 2H, NH_2), 3.09 (q, 2H, CH_2), 1.30 (t, 3H, CH_3), 1.99 ppm (s, 3H, CH_3); IR (KBr, selected bonds): $\nu(N_{amide}–H) = 3553$ (w), 3501 (m-s), 3418 (w-m), 3367 (m-s); $\nu(N_{imine}–H\cdots N) = 3268$ (m, br); $\nu(C–H)$; 1663 (m) $\nu(C{=}N)_{oxime}$ and/or $\nu(C{=}N)_{imine} = 2980$ (m), 2939 (w-m), 2876 (w); $\nu(C{=}N)_{imine}$ and/or $\nu(C{=}N)_{oxime}$ and $\delta(N–H) = 1610$ (vs, br); $\delta(C–H) = 1465$ (m), 1430 (s); $\delta(N_{amide}–H) = 1412$ (s); $\delta(C–H) = 588$ (w), 528 (w-m) cm^{-1}; HRESI-MS: *m/z* calcd for $([2M+NH_4]^+)$: 1208.065; found: 1208.054; elemental analysis (%) calcd for $C_{10}H_{22}N_6Cl_4O_2Pt$: C 20.18, H 3.73, N 14.12; found: C 20.56, H 3.77, N 14.10; TLC (eluent: chloroform/acetone = 8:1, 2:0.25 mL) $R_f = 0.30$; crystals suitable for X-ray diffraction were grown by the slow evaporation in air at RT of a solution in acetone.

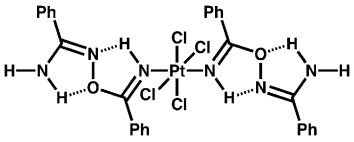


Compound **12**: Yield 91%; m.p. 172 °C (decomp); ^1H NMR (300 MHz, $[D_6]$DMSO, 20 °C): $\delta = 8.55$ (s + d, $^2J_{H,Pt} = 34$ Hz, 1H, NH),

7.4–7.2 (m, 5H, Ph), 7.09 (s, br, 2H, NH_2), 3.47 (s, 2H, CH_2Ph), 3.02 (q, 2H, CH_2), 1.23 ppm (t, 3H, CH_3); IR (KBr, selected bonds): $\nu(N_{amide}–H)$; 3480 (m-s) = 3373 (s); $\nu(N_{imine}–H\cdots N)$ = 3247 (m, br); $\nu(C–H)$ = 3031 (w), 2991 (w), 2943 (w), 2929 (w), 2880 (w); $\nu(C{=}N)_{imine}$ and/or $\nu(C{=}N)_{oxime}$ and $\delta(N–H)$ = 1620 (vs, br); $\delta(C–H)$ = 1496 (m), 1464 (s), 1441 (s); $\delta(N_{amide}–H)$ = 1402 (m); $\delta(C–H)_{Ar}$ = 719 (m), 703 (m); $\delta(C–H)_{Et}$ = 586 (m) cm^{-1}; HRESI-MS: *m/z* calcd for $([2M+H]^+)$: 1495.164; found: 1495.161; calcd for $([2M+Na]^+)$: 1517.146; found: 1517.149; elemental analysis (%) calcd for $C_{22}H_{30}N_6Cl_4O_2Pt$: C 35.35, H 4.05, N 11.24; found: C 35.41, H 4.07, N 11.18; TLC (eluent: chloroform/acetone = 10:1, 2:0.2 mL) R_f = 0.48.

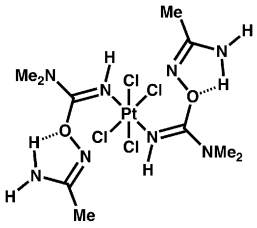


Compound **13**: Yield 84%; m.p. 173 °C (decomp); ^{1}H NMR (300 MHz, [D$_6$]DMSO, 20 °C): δ = 8.67 (s + d, $^2J_{H,Pt}$ = 34 Hz, 1H, NH), 7.8–7.3 (m, 7H, Ph + NH_2), 3.13 (q, 2H, CH_2), 1.29 ppm (t, 3H, CH_3); IR (KBr, selected bonds): $\nu(N_{amide}–H)$ = 3514 (w), 3490 (m), 3408 (w-m), 3371 (m-s); $\nu(N_{imine}–H\cdots N)$ = 3239 (m, br); $\nu(C_{Ar}–H)$; 3064 (vw); $\nu(C–H)(CH_3)$ = 2984 (w), 2921 (w); $\nu(C–H)(CH_2)$ = 2943 (w), 2852 (w); $\nu(C{=}N)_{oxime}$ and/or $\nu(C{=}N)_{imine}$ = 1653 (m); $\nu(C{=}N)_{imine}$ and/or $\nu(C{=}N)_{oxime}$ and $\nu(C{=}C)_{Ar}$ and $\delta(N–H)$ = 1617 (vs, br); $\nu(C{=}C)_{Ar}$ = 1564 (m), 1497 (w); $\nu(C{=}C)_{Ar}$ and $\delta(C–H)_{Et}$ = 1462 (m), 1434 (s); $\delta(N_{amide}–H)$ = 1406 (s); $\delta(C–H)_{Ar}$ = 780 (m), 696 (m-s) cm^{-1}; HRESI-MS: *m/z* calcd for $([M+K]^+)$: 757.010; found: 757.019; $([2M+K]^+)$: 1477.057; found: 1477.070; $([3M+K]^+)$: 2197.104; found: 2197.129; elemental analysis (%) calcd for $C_{20}H_{26}N_6Cl_4O_2Pt$: C 33.39, H 3.64, N 11.68; found: C 33.55, H 3.66, N 11.44; TLC (eluent: chloroform/acetone = 8:1, 2:0.25 mL), R_f = 0.60; crystals suitable for X-ray diffraction were grown by the slow evaporation of a warm (ca. 45 °C) solution in acetone/chloroform.

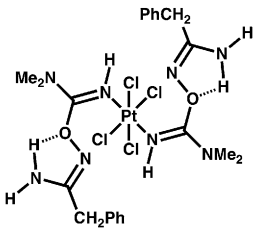


Compound **14**: Yield 72%; m.p. 158 °C (decomp); ^{1}H NMR (300 MHz, [D$_6$]acetone, 20 °C): δ = 9.72 (s, br, 1H, NH), 8.03 (d, 2H, *o*-CH), 7.87 (d, 2H, *o*-CH), 7.65–7.50 (m, 4H, *m*-CH + *p*-CH), 7.45 (t, 2H, *m*-CH), 7.09 ppm (s, br, 2H, NH_2); IR (KBr, selected bonds): $\nu(N_{amide}–H)$ = 3494 (m), 3390 (m-s) ; $\nu(N_{imine}–H\cdots N)$ = 3210 (m, br); $\nu(C_{Ar}–H)$ = 3070 (w), 3058 (w), 3028 (vw); $\nu(C{=}N)_{oxime}$ and/or $\nu(C{=}N)_{imine}$ = 1654 (m); $\nu(C{=}N)_{imine}$ and/or $\nu(C{=}N)_{oxime}$ and $\delta(N–H)$ = 1616 (vs, br); $\nu(C{=}C)_{Ar}$ = 1598 (s), 1565 (m), 1495 (s); $\nu(C{=}C)_{Ar}$ and $\delta(C–H)_{Et}$ = 1450 (m-s); $\delta(N_{amide}–H)$ = 1428 (s, br) cm^{-1}; elemental analysis (%) calcd for $C_{28}H_{26}N_6Cl_4O_2Pt$: C 41.24, H 3.21, N 10.31; found: C 41.16, H 3.42, N 10.30; TLC (eluent: chloroform/acetone = 10:1, 2:0.2 mL) R_f = 0.61; crystals suitable for X-ray diffraction were grown by the slow evaporation in air at RT of a solution in nitromethane.

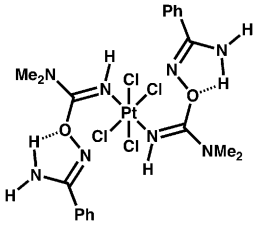
Compound **15**: Yield 79%; m.p. 176 °C (decomp); ^{1}H NMR (300 MHz, [D$_6$]DMSO, 20 °C): δ = 6.37 (s, br, 2H, NH_2), 5.30 (s, br, 1H, NH), 3.02 (s, 6H, NMe_2), 1.76 ppm (s, 3H, CH_3); the signals of Et_2O (1.20, t and 3.48 ppm, q) and $CHCl_3$ (8.32 ppm, s) were detected in the spectrum, their integral intensities are in agreement with the elemental analyses data; IR (KBr, selected bonds): $\nu(N_{amide}–H)$ =



3469 (vs), 3395 (m-s); $\nu(N_{imine}–H)$ = 3360 (m-s); $\nu(C_{Alk}–H)$ = 2968 (w), 2926 (w), 2893 (w), 2872 (vw); $\nu(C{=}N)_{oxime}$ and/or $\nu(C{=}N)_{imine}$ = 1655 (s); $\nu(C{=}N)_{imine}$ and/or $\nu(C{=}N)_{oxime}$ and $\delta(N–H)$ = 1610 (vs); $\delta(C–H)_{Et}$ = 1469 (s); $\delta(C–H)_{NMe}$ = 1426 (m); $\delta(N_{amide}–H)$ = 1406 (s); $\delta(C–H)$ = 623 (w), 592 (m) cm^{-1}; HRESI-MS: *m/z* calcd for $([M-3Cl]^+)$: 519.130; found: 519.122; $([M-Cl]^+)$: 589.068; found: 589.055; $([M+H]^+)$: 625.045; found: 625.030; $([M-Cl+NH{=}C(NMe_2)ON{=}C(NH_2)Me]^+)$: 733.169; found: 733.150; elemental analysis calcd for $C_{10}H_{24}N_8Cl_4O_2Pt\cdot{}^1/_4Et_2O\cdot{}^1/_2CHCl_3$: C 20.06, H 4.00, N 16.63; found: C 19.94, H 4.09, N 16.73; TLC (eluent: chloroform/acetone = 2:1, 2:1 mL) R_f = 0.54; crystals suitable for X-ray diffraction were grown by the slow evaporation in air at RT of a solution in nitromethane.



Compound **16**: Yield 80%; m.p. 165 °C (decomp); ^{1}H NMR (300 MHz, [D$_6$]acetone, 20 °C): δ = 7.40 (d, br, 2H, *o*-CH), 7.34–7.21 (m, 3H, *m*-CH + *p*-CH), 6.15 (s, br, 2H, NH_2), 5.02 (s + d, br, $^2J_{H,Pt}$ = 34 Hz, 1H, NH), 3.46 (s, 2H, CH_2), 3.16 ppm (s, 6H, NMe_2); IR (KBr, selected bonds): $\nu(N_{amide}–H)$ = 3452 (vs), 3398 (s); $\nu(N_{imine}–H)$ = 3334 (vs); $\nu(C_{Ar}–H)$ = 3062 (vw), 3027 (w); $\nu(C–H)_{Alk}$ = 2969 (w), 2933 (w), 2902 (w); $\nu(C{=}N)_{oxime}$ and/or $\nu(C{=}N)_{imine}$ = 1653 (s); $\nu(C{=}N)_{imine}$ and/or $\nu(C{=}N)_{oxime}$ and $\delta(N–H)$ and $\nu(C{=}C)_{Ar}$ = 1610 (vs, br); $\nu(C{=}C)_{Ar}$ = 1494 (m); $\nu(C{=}C)_{Ar}$ and $\delta(C–H)$ = 1471 (m-s, br); $\delta(N_{amide}–H)$ = 1425 (s); $\delta(C–H)_{Ar}$ = 753 (m), 708(s); $\delta(C–H)_{Alk}$ = 630 (m) cm^{-1}; HRESI-MS: *m/z* calcd for $([M-3Cl]^+)$: 671.193; found: 671.190; $([M-H-2Cl]^+)$: 705.154; found: 705.151; $([M-Cl]^+)$: 741.131; found: 799.082; $([M+Na]^+)$: 799.089; found: 741.127; $([M+Na]^+)$: 1577.190; found: 1577.172; elemental analysis calcd for $C_{22}H_{32}N_8Cl_4O_2Pt\cdot2H_2O$: C 32.48, H 4.46, N 13.77, found: C 32.64, H 4.31, N 13.87; TLC (eluent: chloroform/acetone = 10:1, 2:0.2 mL) R_f = 0.64; crystals suitable for X-ray diffraction were grown by the slow evaporation in air at RT of a solution in methanol.



Compound **17**: Yield 85%; m.p. 175 °C (decomp); ^{1}H NMR (300 MHz, [D$_6$]acetone, 20 °C): δ = 7.9–7.65 (m, br, 2H, *o*-CH), 7.6–7.4 (m, 3H, *m*-CH + *p*-CH), 6.59 (s, br, 2H, NH_2), 5.13 (s, br, 1H, NH),

3.24 ppm (s, 6H, NMe_2); IR (KBr, selected bonds): $\nu(N_{amide}–H) = 3462$ (vs), 3400 (s); $\nu(N_{imine}–H) = 3329$ (vs); $\nu(C_{Ar}–H) = 3059$(vw), 3030(vw); $\nu(C–H)_{NMe} = 2977$ (w), 2932 (w), 2879 (w); $\nu(C{=}N)_{oxime}$ and/or $\nu(C{=}N)_{imine} = 1643$ (m); $\nu(C{=}N)_{imine}$ and/or $\nu(C{=}N)_{oxime}$ and $\delta(N–H)$ and $\nu(C{=}C)_{Ar} = 1617$ (vs, br); $\nu(C{=}C)_{Ar} = 1570$ (m), 1491 (m), $\nu(C{=}C)_{Ar}$ and $\delta(C–H)_{Me} = 1469$ (m-s, br); $\delta(N_{amide}–H) = 1400$ (m); $\delta(C–H)_{Ar} = 764$ (m), 701 (s); $\delta(C–H)_{Me} = 606$ (m) cm^{-1}; HRESI-MS: *m/z* calcd for ($[M-3Cl]^+$): 643.162; found: 643.151; ($[M-2Cl]^+$): 678.131; found: 678.120; ($[M-Cl]^+$): 713.099; found: 713.086; ($[M+H]^+$): 749.076; found: 749.063; ($[M+Na]^+$): 771.058; found: 771.040; ($[M+K]^+$): 787.032; found: 784.017; elemental analysis calcd for $C_{20}H_{28}N_8Cl_4O_2Pt$: C 32.06, H 3.77, N 14.95; found: C 32.06, H 4.07, N 14.91; TLC (eluent: chloroform/acetone = 10:1, 2:0.2 mL) $R_f = 0.54$; crystals suitable for X-ray diffraction were grown by the slow evaporation in air at RT of a solution in acetone or in chloroform.

Compounds **7**, **8**, and **11**–**17** are air stable at RT in the solid state and in the most common organic solvents. These species are also stable in nitromethane at reflux for at least 2 h (**11**–**17**), meanwhile **7** and **8** decompose under these conditions for 2 h. Complex **10** degrades in common organic solvents after three weeks at 20–25 °C or after 45 min in nitromethane at reflux to produce a broad range of yet unidentified species. Complex **9** could not be crystallized and it decomposes within 6 h at RT to form oily residues. Complex **9** could not be purified from the hydrolysis products and was characterized in a mixture. No molecular ion of **14** or its fragmentation was observed in the mass spectrum despite running the experiment in a wide interval of voltage at capillary exit and using different solvents (MeOH, CH_2Cl_2, and MeCN) and mixtures of them.

Liberation of the iminoacylated amidoximes

A mixture of an imino complex (**11**–**17**; 0.06 mmol) and NaCN (17.7 mg, 0.36 mmol) were dissolved in [D_6]DMSO (0.56 mL) at RT to produce **19**–**25**, respectively. The completeness of the liberation was monitored by ^{1}H NMR spectroscopy. The product was detected by ^{1}H NMR spectroscopy after 5 min, whereupon it was characterized by $^{13}C\{^1H\}$ NMR technique (total acquisition time is ca. 2 h). Besides [D_6]DMSO signals, high resolution ESI-MS spectra exhibited signals of quasimolecular ions of amidoximes **6**, **5**, and **4** (for **19**–**21** and **23**–**25**, respectively; and **4** for **22**) and dimethyl urea (for **23**–**25**).

Compound **19**: 100% yield based on ^{1}H NMR data; half-decay period is about 8 days; ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): $\delta =$ 7.57 (s, br, 1H, NH), 6.31 (s, br, 2H, NH_2), 2.16 (q, 2H, CH_2), 1.76 (s, 3H, CH_3), 1.08 ppm (t, 3H, CH_3); ^{13}C NMR (75 MHz, [D_6]DMSO, 20 °C): $\delta = 167.51$ (*C*(Et)(O)(=NH)), 158.23 (*C*(CH_3)(NH_2)(=N)), 26.17 (*C*H_2), 20.17 (*C*H_3), 11.05 ppm (*C*H_3).

Compound **20**: 100% yield based on ^{1}H NMR data; half-decay period is about 6 days. ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): $\delta =$ 7.59 (s, br, 1H, NH), 7.40–7.15 (m, 5H, Ph), 6.43 (s, br, 2H, NH_2), 3.45 (s, 2H, CH_2), 2.17 (q, 2H, CH_2), 1.07 ppm (t, 3H, CH_3); ^{13}C NMR (75 MHz, [D_6]DMSO, 20 °C): $\delta = 168.75$ (*C*(Et)(O)(=NH)), 157.91 (*C*(CH_2Ph)(NH_2)(=N)), 137.89 (*ipso*-C), 129.54 (*m*-*C*H), 129.10 (*o*-*C*H), 127.42 (*p*-*C*H), 37.67 (*C*H_2Ph), 25.91 (*C*H_2), 11.43 ppm (*C*H_3).

Compound **21**: 100% yield based on ^{1}H NMR data; half-decay period is about 5 days; ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): $\delta =$ 7.82 (s, br, 1H, NH), 7.75 (d, 2H, *o*-CH), 7.5–7.4 (m, 3H, *m*-CH + *p*-CH), 6.76 (s, br, 2H, NH_2), 2.26 (q, 2H, CH_2), 1.13 ppm (t, 3H, CH_3); ^{13}C NMR (75 MHz, [D_6]DMSO, 20 °C): $\delta = 168.42$ (*C*(Et)(O)(=NH)), 156.00 (*C*(Ph)(NH_2)(=N)), 132.64 (*ipso*-C), 131.24 (*p*-*C*H), 129.24 (*o*-*C*H), 127.47 (*m*-*C*H), 25.91 (*C*H_2), 11.52 ppm (*C*H_3).

Compound **22**: 100% yield based on ^{1}H NMR data; half-decay period is about 6 days. ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): $\delta =$ 8.41 (s, br, 1H, NH), 8.19 (d, 2H, *o*-CH), 7.84 (d, 2H, *o*-CH), 7.55–7.40 (m, 6H, *m*-CH + *p*-CH), 7.02 ppm (s, br, 2H, NH_2); ^{13}C NMR (75 MHz, [D_6]DMSO, 20 °C): $\delta = 162.25$ (*C*(Ph)(O)(=NH)), 162.22 (*C*(Ph)(NH_2)(=N)), 156.31 (*p*-*C*H), 132.68 (*p*-*C*H), 131.79 (*ipso*-C), 131.35 (*ipso*-C), 129.28 (*o*-*C*H), 128.99 (*o*-*C*H), 128.57 (*m*-*C*H), 127.69 ppm (*m*-*C*H).

Compound **23**: 100% yield based on ^{1}H NMR data; half-decay period is about 7 min. ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): $\delta = 7.02$ (s, br, 1H, NH), 6.54 (s, br, 1H, NH), 5.65 (s, br, 1H, NH), 3.29 (s, 6H, NMe_2), 1.82 ppm (s, 3H, CH_3); ^{13}C NMR was not obtained because of fast decomposition of the imine in solution.

Compound **24**: 100% yield based on ^{1}H NMR data; half-decay period is about 7 min. ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): $\delta =$ 7.40–7.17 (m, 5H, Ph), 6.69 (s, br, 1H, NH), 6.36 (s, br, 1H, NH), 5.72 (s, br, 1H, NH), 3.45 (s, 2H, CH_2), 3.29 ppm (s, 6H, NMe_2); ^{13}C NMR was not obtained because of fast decomposition of the imine in solution.

Compound **25**: 100% yield based on ^{1}H NMR data; half-decay period is about 7 min. ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): $\delta = 7.74$ (d, 2H, *o*-CH), 7.66–7.35 (m, 3H, *m*-CH + *p*-CH), 7.18 (s, br, 2H, NH_2), 5.86 (s, br, 1H, NH), 3.36 ppm (s, 6H, NMe_2); ^{13}C NMR was not obtained because of fast decomposition of the imine in solution.

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