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Stereoselective [2 + 3] cycloaddition of nitrones to platinum-bound organonitriles. First enantioselective synthesis of Δ^4-1,2,4-oxadiazolines †

Gabriele Wagner *[a] **and Matti Haukka** [b]

[a] *Instituto de Tecnologia Química e Biológica, Universidade Nova de Lisboa, Av. da República, Apartado 127, 2781-901 Oeiras, Portugal*
[b] *Department of Chemistry, University of Joensuu, P.O. Box 111, FIN-80101 Joensuu, Finland*

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Coordinated benzonitrile in *cis*-[$PtCl_2(R^3MeSO)(PhCN)$] (R^3 = Me, Ph) is sufficiently activated to undergo [2 + 3] cycloaddition with nitrones $^-O^+N(R^2)=CH(R^1)$ (R^1 = Ph, *p*-C_6H_4Me, *p*-C_6H_4OMe, R^2 = Me; R^1 = Ph, R^2 = CH_2Ph) under mild conditions to give the corresponding Δ^4-1,2,4-oxadiazoline complexes *cis*-[$PtCl_2(R^3MeSO)$-{N=C(Ph)–ON(R^2)–CH(R^1)}] in 68–83% yield. In this reaction, the chiral sulfoxide in *cis*-[$PtCl_2$(PhMeSO)(PhCN)] induces stereoselective formation of the coordinated Δ^4-1,2,4-oxadiazoline leading to mixtures of diastereomeric platinum complexes with a d.e. of 30–60%, which can be enhanced to >90% by fractional crystallization. The major diastereoisomer of [$PtCl_2$(PhMeSO){N=C(Ph)–ON(Me)–C(H)Ph}] thus obtained was analyzed by X-ray diffraction and shown to have *cis*-(*R*,*S*) configuration.

Reaction of *cis*-[$PtCl_2(R^3MeSO)${N=C(Ph)–ON(R^2)–CH(R^1)}] with ethane-1,2-diamine results in displacement of the Δ^4-1,2,4-oxadiazolines from the metal and concomitant formation of water-soluble $[Pt(en)_2]Cl_2$ and sulfoxide, which can both be removed by aqueous extraction, and this allows for the first time the isolation of Δ^4-1,2,4-oxadiazolines in enantiomerically enriched form. Applying this technique to *cis*-(R_S,S_C)-[$PtCl_2$(PhMeSO)-{N=C(Ph)–ON(Me)–C(H)Ph}] of 90% d.e. and 79% e.e. in sulfoxide, the corresponding (*R*)-2-methyl-3,5-diphenyl-Δ^4-1,2,4-oxadiazoline was obtained with 70% e.e.

Introduction

Activation of organic molecules by coordination to a metal center has become a widespread technique in inorganic and organic synthesis in order to achieve reactions which are not feasible or uncommon for the corresponding non-coordinated species.[1] In this context, activation of nitriles towards nucleophilic attack received much attention[2] and especially platinum complexes proved to be useful substrates for this kind of transformation involving a wide variety of nucleophiles such as oximes,[3] hydroxylamines,[4] alcoholates,[5] hydroxide,[6] ammonia,[7] amines,[8] carbanions,[9] phosphorous ylides,[10] or thiols.[11] In spite of the high potential of this method, the enhanced reactivity of platinum-coordinated nitriles was only rarely used for cyclization reactions, and only some examples of the addition of chloroalkoxides to give coordinated oxazolines[12] or 1,3-oxazines,[13] or the reaction with aziridines to form coordinated amidines which, upon release from the metal center, cyclize to give the corresponding imidazolines, are found in the literature.[14]

In the course of our recent studies on the synthesis of heterocycles *via* metal-mediated reactions of coordinated nitriles, we concentrated on the [2 + 3] cycloaddition of nitrones to nitriles. This reaction, although known in organic chemistry as the only method for the preparation of Δ^4-1,2,4-oxadiazolines, is highly restricted to nitriles bearing a strongly electron withdrawing substituent (*e.g.* CCl_3) but can be easily achieved under very mild conditions with electron-rich nitriles like MeCN or PhCN when they are bound to Pt(IV) centers.[15] In contrast, Pt(II) was found to exhibit a slightly lesser extent of activation, leading to a selective transformation of coordinated PhCN but not MeCN.[16] The corresponding platinum Δ^4-1,2,4-oxadiazoline complexes were obtained as air-stable compounds in high yields, and displacement of the newly formed ligand from both Pt(IV) or Pt(II) compounds was readily achieved, thus allowing us to use this method in the preparation of heterocycles with substitution patterns that were not previously accessible by organic methods.

However, coordination to a metal center does not only change the reactivity of a ligand but can also modify the stereochemical outcome of a reaction, depending on the sterical requirements of additional ligands coordinated to a given metal site. Applied to the reaction described above in which a new stereocenter is generated on the oxadiazoline N–*C*HR–N carbon, one might expect that the chiral center of the first oxadiazoline formed has an influence on the stereochemical course of the addition of the second nitrone, thus leading to an unequal distribution of the (*R*,*S*) and (*R*,*R*)/(*S*,*S*) diastereoisomers in the final product. However, for both *trans*-Pt(IV) and *trans*-Pt(II) complexes, we found formation of the corresponding diastereoisomers in a ratio of 1 : 1 (d.e. = 0%), indicating that the chiral oxadiazoline in the *trans* position on the metal is not efficient in inducing stereoselection (see Scheme 1).

Due to the importance of enantiomerically pure platinum complexes and heterocyclic compounds in pharmaceutical chemistry, and additionally due to the fact that, up until now, there was no known method of synthesis for enantiomerically pure or enriched Δ^4-1,2,4-oxadiazolines in organic chemistry, we found it worthwhile to concentrate on improving the stereoselectivity of the previously found reaction, and our results

† Electronic supplementary information (ESI) available: rotatable 3-D crystal structure diagram in CHIME format. See http://www.rsc.org/suppdata/dt/b1/b102291c/

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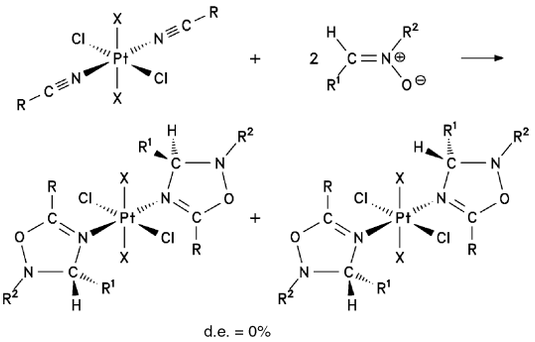


Scheme 1 [2 + 3] Cycloaddition of nitrones to Pt(IV)- or Pt(II)-bound organonitriles (X = Cl, —; see refs. 15 and 16).

leading to the first enantioselective synthesis of Δ^4-1,2,4-oxadiazolines *via* diastereoselective synthesis of Pt(oxadiazoline) complexes are presented in this paper.

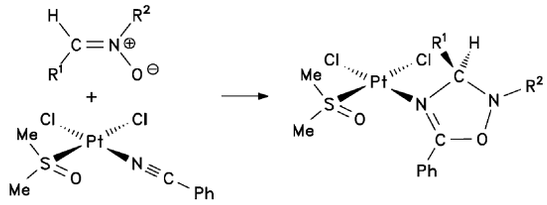
Results and discussion

For the present study, we addressed complexes of the type [$PtCl_2$(sulfoxide)(PhCN)] for the following reasons: (*i*) Our previous studies showed that the coordinated benzonitrile in *trans*-[$PtCl_2(PhCN)_2$] is indeed sufficiently activated towards reaction with nitrones to give Δ^4-1,2,4-oxadiazoline complexes.[16] (*ii*) Sulfoxides were chosen as auxiliary ligands because they are expected to be unreactive towards nitrones and are easily available in enantiopure or at least enantiomerically enriched form by known organic,[17] metal-catalyzed[18] or biotechnological methods.[19] (*iii*) Complexes of the type [$PtCl_2$-(sulfoxide)(RCN)] are easily accessible and various routes for their preparation are described in the literature.[20] (*iv*) Additionally, in most of the [$PtCl_2$(sulfoxide)(nitrile)] complexes known, the sulfoxide and nitrile ligands are *cis* to each other.[21] This will ensure steric interaction of the substituents of the sulfoxide with the nitrone during the course of cycloaddition and therefore, a stereochemical induction can be expected. Our assumption is supported by some early reports on stereoselectivity in Pt complexes describing the optical resolution of a sulfoxide *via* diastereomeric Pt(sulfoxide)(amine) complexes,[22] interligand recognition between prochiral olefin and chiral sulfoxide coordinated to platinum,[23] or, more recently, the enantiomeric discrimination in the formation of (*R*,*S*)- *vs.* (*R*,*S*)/(*S*,*S*)-*cis*-[$PtCl_2(R^1R^2SO)_2$],[24] or the use of Pt(amine) complexes as chiral derivatizing agents for the determination of the enantiomeric composition of allylic alcohols and ethers.[25]

Cycloaddition reaction of *cis*-[$PtCl_2$(dmso)(PhCN)]

In order to explore first the *reactivity* of the mixed sulfoxide/benzonitrile complexes towards cycloaddition of nitrones, we have chosen *cis*-[$PtCl_2$(dmso)(PhCN)] whose synthesis was performed according to published methods.[26] Cycloaddition of nitrones $^-O^+N(Me)=CH(R^1)$ (R^1 = Ph, *p*-C_6H_4Me, *p*-C_6H_4-OMe) to the coordinated benzonitrile occurs at room temperature within two days or at 50 °C overnight to give the corresponding *cis*-[$PtCl_2$(dmso)(oxadiazoline)] complexes in 78–83% isolated yield (see Scheme 2).

The identity of the products was confirmed by elemental analysis, FAB mass spectrometry, IR and ^{1}H, $^{13}C\{^1H\}$ and ^{195}Pt NMR spectroscopy. In the IR spectra, disappearance of the C≡N vibration at 2292 cm^{-1} was accompanied by the appearance of a new intense band for the C=N stretching in a range 1630–1638 cm^{-1} which is in good agreement with the values found for the previously described [$PtCl_2$(oxadiazoline)$_2$] complexes (1622–1660 cm^{-1}).[16] The S=O stretching vibration of the sulfoxide is shifted only moderately to lower wavenumbers (1126–1139 cm^{-1}) as compared to the starting material (1145 cm^{-1}).



Scheme 2 [2 + 3] Cycloaddition of nitrones to [$PtCl_2$(dmso)(PhCN)] (R^1 = Ph, *p*-C_6H_4Me, *p*-C_6H_4OMe, R^2 = Me; R^1 = Ph, R^2 = CH_2Ph).

In the ^{1}H and $^{13}C\{^1H\}$ NMR spectra, characteristic signals of the oxadiazoline ligands appear at very similar chemical shifts as observed for the corresponding [$PtCl_2$(oxadiazoline)$_2$] complexes.[16] In contrast to the starting complex [$PtCl_2$(dmso)-(PhCN)] which shows only one signal for the Me groups of the coordinated dmso (3.56 ppm, J_{PtH} 21 Hz), the reaction products [$PtCl_2$(dmso)(oxadiazoline)] display the sulfoxide methyl groups as two signals of significantly different chemical shift (2.55–2.68 ppm and 2.75–2.76 ppm, J_{PtH} 14.0–20.4 Hz) as a result of restricted rotation of the sulfoxide around the Pt–S bond due to the neighbouring bulky oxadiazoline ligand. The higher shielding of both Me groups may be due to the influence of the magnetic anisotropy of the phenyl substituents of the oxadiazoline. In addition, strong NOE effects are observed between the dmso methyl group with lower ^{1}H chemical shift and the aromatic protons of the oxadiazoline, and all these arguments give evidence for the *cis* geometry of these complexes. Additional support is given by the ^{195}Pt signal which appears at −2956 to −2964 ppm, well in the range found for other *cis*-Pt(II)(dmso)(imine) complexes described in the literature.[27]

When the sterically more demanding nitrone $^-O^+N(CH_2Ph)$=C(H)(Ph) is used, the formation of two isomeric products in a ratio 90 : 10 is observed. General features of the major product are the same as described above for the sterically less demanding nitrones and therefore we assign the *cis*-geometry to this isomer. The minor isomer, which is also visible by TLC as a separate spot with a higher R_f value, shows ^{1}H and ^{13}C signals typical for the oxadiazoline ligand but exhibits only one signal for the two methyl groups of the dmso ligand (3.47 ppm in ^{1}H, 44.4 ppm in ^{13}C). As irradiation into this singlet does not generate any NOE with other signals, we attribute *trans*-geometry to this isomer. The ^{195}Pt signal at a more negative value (−3087 ppm) confirms this assignment insofar as the same trend of chemical shift and a similar $\Delta\delta$ was observed for a series of Pt(II)(sulfoxide)(nitrile) complexes.[28]

The results described in this section show that, in accord with our expectations, the activation of the nitrile in [$PtCl_2$-(sulfoxide)(PhCN)] is sufficiently high and of the same order as previously described for the corresponding reactions of [$PtCl_2(PhCN)_2$].[16] The sulfoxide indeed neither interferes by reacting itself nor modifies the *reactivity* of the coordinated benzonitrile. In addition, the sulfoxide remains coordinated in the *cis* position during the course of the cycloaddition reaction, at least as long as only moderately bulky nitrones are used as reagents, and therefore, an extension of this study to complexes bearing a chiral sulfoxide instead of dmso seems worthwhile.

Cycloaddition reaction of racemic *cis*-[$PtCl_2$(PhMeSO)(PhCN)]

Racemic [$PtCl_2$(PhMeSO)(PhCN)] was prepared by an analogous method to the synthesis of the corresponding dmso complex[26] and obtained as the pure *cis*-isomer, as confirmed by the appearance of only one set of signals in the ^{1}H- and $^{13}C\{^1H\}$-NMR spectra and only one ^{195}Pt-NMR resonance at −3007 ppm which is well in the range found for similar compounds described in the literature.[28] Cycloaddition of the nitrones $^-O^+N(Me)=CH(R^1)$ (R^1 = Ph, *p*-C_6H_4Me, *p*-C_6H_4-OMe) to this compound occurs under the same conditions described in the previous section for the corresponding dmso

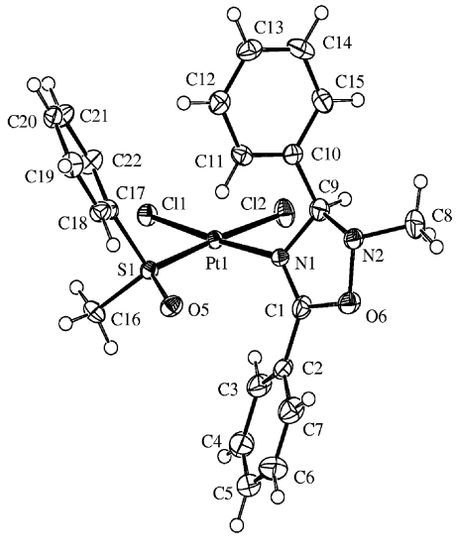


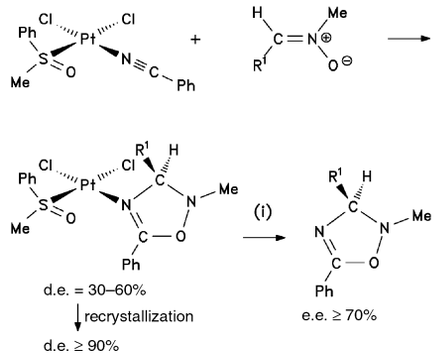
Fig. 1 The molecular structure of racemic *cis*-(*R*,*S*)/(*S*,*R*)-[$PtCl_2$(PhMeSO){N=C(Ph)O–N(Me)–C(H)Ph}] with atomic numbering scheme. Only the (R_S,S_C)-enantiomer is shown.

complex and gives, after chromatographic workup, a mixture of two diastereomeric *cis*-[$PtCl_2$(PhMeSO)(oxadiazoline)] complexes in ratios 80 : 20 (for R^1 = Ph, d.e. = 60%), 70 : 30 (for R^1 = *p*-C_6H_4Me, d.e. = 40%) and 65 : 35 (for R^1 = *p*-C_6H_4OMe, d.e. = 30%). The major diastereoisomers were obtained in pure form (d.e. > 90%) by fractional crystallization from $CHCl_3$–diethyl ether and the molecular structure of the corresponding [$PtCl_2$(PhMeSO){N=C(Ph)O–N(Me)–C(H)Ph}] complex was determined by X-ray diffraction analysis (Fig. 1).

The centrosymmetric crystal is composed from racemic pairs of molecules with the (R_S,S_C) and (S_S,R_C) configuration. The coordination sphere around platinum is slightly distorted square-planar with the sulfoxide and oxadiazoline ligands in *cis* positions to each other. The oxadiazoline ring adopts a twisted conformation similar to the one already observed in the previously described Pt(IV) [15] and Pt(II) complex [16] and also in a few known examples of structurally characterized uncoordinated Δ^4-1,2,4-oxadiazolines.[29] The methyl group on N(2) and the axial hydrogen on the chiral carbon atom C(9) both point away from the sulfoxide whereas the equatorial phenyl substituent on C(9) is directed towards the phenyl of the sulfoxide, but no evidence is found for a mutual interaction between these aromatic rings. The sulfoxide oxygen as the sterically least demanding substituent on sulfur is oriented towards the oxadiazoline ring and deviates from the Pt coordination plane by only −0.42 Å. The methyl substituent of the sulfoxide points to the same side of the Pt coordination plane as the oxadiazoline N=C(Ph)–O unit, but no close contacts occur between the ligands. In total, the structure exhibits all bond lengths and angles (Table 1) in the normal range,[30] and no steric strains are present (Scheme 3).

The isolated products, pure (R_S,S_C)/(S_S,R_C) diastereoisomers as well as the diastereomeric mixtures, were also characterized by standard analytic and spectroscopic methods. Elemental analyses, FAB mass-spectra and the typical IR absorptions of the oxadiazoline C=N at 1622–1628 cm^{-1} and the sulfoxide S=O at 1136–1142 cm^{-1} confirm the description of the products as [$PtCl_2$(PhMeSO)(oxadiazoline)] complexes.

^1H and $^{13}C\{^1H\}$ spectra of both diastereoisomers display the expected signals of the sulfoxide and oxadiazoline units, but mainly the proton chemical shifts reflect characteristic features corresponding to the different stereochemistry of the complexes. The signal of the N–C*H*–N of the major isomer is found at slightly lower chemical shift (5.93–6.03 ppm) than that of the minor isomer (6.05–6.19 ppm). More pronounced



Scheme 3 Diastereoselective [2 + 3] cycloaddition to [$PtCl_2$(PhMeSO)(PhCN)] (R^1 = Ph, *p*-C_6H_4Me, *p*-C_6H_4OMe) and liberation of the ligand. (i): 1) ethane-1,2-diamine, 2) H_2O.

Table 1 Selected bond lengths (Å) and angles (°) for *cis*-(*R*,*S*)/(*S*,*R*)-[$PtCl_2$(PhMeSO){N=C(Ph)O–N(Me)–C(H)Ph}]

Pt(1)–Cl(1)	2.2934(8)	O(6)–C(1)	1.339(4)
Pt(1)–Cl(2)	2.3168(9)	N(1)–C(1)	1.291(4)
Pt(1)–S(1)	2.2261(8)	N(1)–C(9)	1.470(4)
Pt(1)–N(1)	2.045(3)	N(2)–C(8)	1.478(5)
S(1)–O(5)	1.467(2)	N(2)–C(9)	1.472(4)
S(1)–C(16)	1.779(3)	C(1)–C(2)	1.469(5)
S(1)–C(17)	1.794(3)	C(9)–C(10)	1.498(5)
O(6)–N(2)	1.478(4)		
Cl(1)–Pt(1)–Cl(2)	88.22(3)	O(6)–N(2)–C(8)	105.4(3)
Cl(1)–Pt(1)–S(1)	92.87(3)	O(6)–N(2)–C(9)	103.5(2)
Cl(1)–Pt(1)–N(1)	174.93(8)	C(8)-N(2)–C(9)	112.2(3)
Cl(2)–Pt(1)–S(1)	177.04(3)	O(6)–C(1)–N(1)	115.1(3)
Cl(2)–Pt(1)–N(1)	86.93(8)	O(6)–C(1)–C(2)	114.7(3)
S(1)–Pt(1)–N(1)	92.04(8)	N(1)–C(1)–C(2)	130.2(3)
Pt(1)–S(1)–O(5)	115.09(10)	C(1)–C(2)–C(3)	122.0(3)
Pt(1)–S(1)–C(16)	111.22(12)	C(1)–C(2)–C(7)	117.5(3)
Pt(1)–S(1)–C(17)	112.54(11)	N(1)–C(9)–N(2)	102.5(3)
O(5)–S(1)–C(16)	107.76(16)	N(1)–C(9)–C(10)	116.5(3)
O(5)–S(1)–C(17)	107.29(15)	N(2)–C(9)–C(10)	109.3(3)
C(16)–S(1)–C(17)	102.03(16)	C(9)–C(10)–C(11)	122.4(3)
N(2)–O(6)–C(1)	104.9(2)	C(9)–C(10)–C(15)	118.0(3)
Pt(1)–N(1)–C(1)	130.8(2)	S(1)–C(17)–C(18)	116.7(2)
Pt(1)–N(1)–C(9)	120.2(2)	S(1)–C(17)–C(22)	121.9(3)
C(1)–N(1)–C(9)	107.7(3)		

differences appear in the aromatic range where the major diastereoisomer shows characteristic exposed doublets, one on the high-field end and another one on the low-field end of the aromatic range (6.43–6.99 ppm, 8.80–8.89 ppm), reflecting a stronger magnetic interaction of the aromatic rings in this complex. The minor isomer, in contrast, exhibits all aromatic signals at more balanced chemical shifts (between 7.05 and 8.49 ppm), suggesting that the aromatic rings in this compound keep a larger average distance from each other in solution. Similar observations are made even for the rather peripheral substituents in the *para* position of R^1, whose signals appear at unusually low δ values in the major isomer (2.07 for C_6H_4*Me*, 3.60 for C_6H_4O*Me*), whereas the corresponding signals of the minor isomer are in the normal range (2.40 for C_6H_4*Me*, 3.83 for C_6H_4O*Me*).

The ^{195}Pt NMR signal of the major diastereoisomer appears in a range of −2975 to −2982 ppm, whereas the signal of the minor product is found *ca.* 50 ppm downfield at −2928 to −2930 ppm. Similar differences in chemical shift were already observed between the (+/−)- and *meso*-forms of *cis*-[$PtCl_2$(PhMeSO)$_2$] [24] or for diastereomeric Pt(amine) complexes [31] and therefore, we conclude that the minor isomer is indeed the *cis*-(*R*,*R*)/*cis*-(*S*,*S*) diastereoisomer and not a *trans*-isomer for which an upfield-shift of *ca.* 130 ppm would be expected. Additional support for our conclusion is given by the fact that both isomers elute from silica gel with practically the same R_f value and only one spot is detected on TLC. If the two

compounds were a *cis*/*trans* isomeric pair, one should expect two spots due to the different polarity of such isomers, as was indeed observed for the closely related complex *cis*/*trans*-[$PtCl_2(Me_2SO)${N=C(Ph)–ON(CH_2Ph)–C(H)Ph}] described in the previous section.

Cycloaddition reaction of enantiomerically enriched *cis*-[$PtCl_2$(PhMeSO)(PhCN)]

The considerable diastereoselectivity with which the racemic *cis*-[$PtCl_2$(PhMeSO)(oxadiazoline)] complexes are formed, together with the possibility of isolating their major diastereoisomers in practically pure form by recrystallization, makes it worthwhile to extend the present study to optically active complexes, as only in this case will optically active oxadiazolines be formed. For this purpose, enantiomerically enriched (*S*)-PhMeSO (e.e. = 79%, as confirmed by optical rotation)[32] was synthesized by oxidation of thioanisole with an enantiopure camphor-derived oxaziridine {IUPAC-name: (4*aS*),(9*aR*)-10,10-dimethyl-6,7-dihydro-4*H*-4a,7-methano-oxaziridino[3,2-j]-oxepino[3,4-c]isothiazol-9(5*H*)-one-3,3-dioxide} according to the literature.[33] The complex (*R*)-*cis*-[$PtCl_2$(PhMeSO)(PhCN)] prepared therefrom was used for the analogous cycloaddition experiments and gave the corresponding diastereomeric *cis*-[$PtCl_2$(PhMeSO)(oxadiazoline)] complexes with the same yields and d.e. as previously described for the racemic compounds. This observation is worthwhile to note in this context, as it suggests that the diastereoselection is indeed due to a kinetic differentiation in the course of cycloaddition and not to thermodynamic equilibration of the product complexes by ligand exchange which would lead to a different d.e. for the racemic or enantiomerically enriched samples.

Liberation of Δ^4-1,2,4-oxadiazolines from the platinum(II) complexes and determination of the enantiomeric excess

In order to use the synthetic procedure described in the previous section as a method for the enantioselective preparation of Δ^4-1,2,4-oxadiazolines, the newly formed heterocycle has to be displaced from the metal in a way that allows for convenient isolation. This can be achieved under very mild conditions by stirring a chloroform solution of the individual [$PtCl_2$(sulfoxide)(oxadiazoline)] complexes with an excess of ethane-1,2-diamine (5 equivalents). Reaction at room temperature is complete within 1–2 h and gives a mixture of free oxadiazoline, free sulfoxide and a white precipitate of the well known [$Pt(en)_2$]Cl_2.[34] The unreacted ethane-1,2-diamine and both sulfoxide and the cationic platinum complex are extracted quantitatively with water and were identified by ^{1}H, ^{13}C{^{1}H} and ^{195}Pt NMR in the aqueous phase {^{195}Pt NMR: −3042 ppm, lit.[34] for [$Pt(en)_2$]Cl_2: −3036 ppm}. The oxadiazoline remaining as the only compound in the organic phase is easily isolated in 74–91% yield by evaporation of the solvent. Alternatively, chromatography of the crude reaction mixture on SiO_2–CH_2Cl_2 can be used for separation, with the advantage that the purity of the oxadiazoline is slightly improved.

The isolated oxadiazolines were characterized by IR (film), ^{1}H and ^{13}C{^{1}H} NMR spectra and all data were found in the expected range (see Experimental). In cases where either racemic or enantiomerically enriched *cis*-(R_S,S_C)-[$PtCl_2$(PhMeSO){N=C(Ph)–ON(Me)–C(H)Ph}] of 90% d.e. and 79% e.e. in sulfoxide were used for their synthesis, the enantiomeric composition of the isolated oxadiazoline was determined by ^{1}H NMR using [Eu(hfc)$_3$] {tris-[3-(heptafluoropropyl-hydroxymethylene)-(+)-camphorato]europium} as chiral paramagnetic shift reagent. The splitting of the signal of the N–C*H*(R^1)–N group allows for separate integration of the two enantiomers and thus confirmed that the racemic complex indeed releases racemic 2-methyl-3,5-diphenyl-Δ^4-1,2,4-oxadiazoline, whereas the same heterocycle liberated from the enantiomerically enriched complex was obtained with an e.e. of 70%. This confirms on the one hand that the e.e. of the oxadiazoline can be predicted from the d.e. of the complex and the e.e. of the sulfoxide, and additionally suggests that Δ^4-1,2,4-oxadiazolines are configurationally stable under the conditions used for displacement and isolation, and therefore, the method proposed in this work might be generally applicable for the enantioselective synthesis of such kind of compounds.

Concluding remarks

Extending our previously described method of platinum-mediated [2 + 3] cycloaddition of nitrones to nitriles now to chiral Pt(II) compounds, diastereoselective formation of Pt-(oxadiazoline) complexes was achieved and a facile method for the release of the heterocyclic ligand and its isolation was developed. This technique, applied to enantiomerically enriched material, gives for the first time enantioselective access to Δ^4-1,2,4-oxadiazolines with e.e. up to 70%, and their absolute configuration was established by X-ray analysis of the parent platinum complex.

The proposed method is experimentally highly convenient, using easily accessible starting materials, working under mild reaction conditions and avoiding technically complicated or expensive processes (*e.g.* inert gas atmosphere, extreme temperature or pressure) which are often required for Lewis acid promoted reactions involving other metals. All these advantages, together with the possibility for recycling platinum almost quantitatively after use, compensate for the disadvantage of a stoichiometric application of a precious metal.

The obtained stereoselectivity is considerable for a first study in this field, nevertheless, further studies using other chiral auxiliary ligands are being performed in our team in order to improve the diastereoselectivity of the cycloaddition and simultaneously gain more insight into the factors governing the preferential formation of one of the possible diastereoisomeric complexes. This might finally allow us to predict which enantiomer of the oxadiazoline will be formed when a new chiral auxiliary is used.

Experimental

Materials and instrumentation

All reactions were carried out in commercial solvents without the use of an inert atmosphere. PhMeSO was prepared by oxidation of thioanisole as described,[33,35] the chiral oxidizing agent (4*aS*),(9*aR*)-10,10-dimethyl-6,7-dihydro-4*H*-4a,7-methano-oxaziridino[3,2-j]oxepino[3,4-c]isothiazol-9(5*H*)-one-3,3-dioxide was obtained according to the literature.[33] Nitrones were synthesized by condensation of the corresponding aldehyde and *N*-alkylhydroxylamine following published methods.[36] *cis*-[$PtCl_2$(dmso)(PhCN)][26] was prepared as previously described. C, H and N elemental analyses were carried out by the Microanalytical Services of the Instituto Superior Técnico and Instituto de Tecnologia Química e Biológica. Melting points were determined with a Büchi 530 apparatus in open capillaries. Optical rotations were measured on an Atago Polax-2L polarimeter. For TLC, Merck UV 254 SiO_2-plates have been used. Positive-ion FAB mass spectra were obtained on a Trio 2000 instrument by bombarding 3-nitrobenzyl alcohol (NBA) matrices of the samples with 8 keV (*ca.* 1.28×10^{-15} J) Xe atoms. Mass calibration for data system acquisition was achieved using CsI. Infrared spectra (4000–400 cm^{-1}) were recorded on BIO-RAD FTS 3000MX and Mattson 7000 FTIR instruments in KBr pellets (Pt-complexes) or films (oxadiazolines). ^{1}H, ^{13}C{^{1}H}, and ^{195}Pt NMR experiments were performed on Varian UNITY 300 and Bruker AMX300 spectrometers at ambient temperature. ^{195}Pt chemical shifts are

Table 2 Crystallographic data for *cis*-(*R*,*S*)/(*S*,*R*)-[$PtCl_2$(PhMeSO){N=C(Ph)O–N(Me)–C(H)Ph}]

Empirical formula	$C_{22}H_{22}N_2Cl_2O_2PtS$
FW	644.47
T/K	150(2)
λ/Å	0.71073
Space group	$P\bar{1}$ (no. 2)
a/Å	9.5957(2)
b/Å	9.7390(2)
c/Å	12.1048(2)
α/°	79.930(1)
β/°	87.593(1)
γ/°	86.115(1)
V/Å^3	1110.71(4)
Z	2
ρ_{calcd}/g cm^{-3}	1.927
μ(Mo-Kα)/mm^{-1}	6.673
R_1 [a]	0.0214
wR_2 [b]	0.0522

[a] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$.

given relative to aqueous $K_2[PtCl_4]$ = −1630 ppm, with half height line width in parentheses.

X-Ray structure determination of *cis*-[$PtCl_2$(PhMeSO)-{N=C(Ph)O–N(Me)–C(H)Ph}]

Crystals suitable for structural analysis were grown as colourless plates by diffusion of diethyl ether into a $CHCl_3$ solution of the complex. X-Ray diffraction data of a colourless plate of 0.20 × 0.10 × 0.10 mm size were collected with a Nonius KappaCCD diffractometer using Mo-Kα radiation (λ = 0.71073 Å) and φ-scan data collection mode with a Collect[37] data collection program. Denzo and Scalepack[38] programs were used for cell refinements and data reduction. A multi-scan absorption correction, based on equivalent reflections (XPREP in SHELXTL v. 5.1[39]), was applied to the data (T_{max}/T_{min} was 0.2233/0.3595). The structure was solved by Patterson methods using the DIRDIF-99 program.[40] Structure refinement (full-matrix least-squares on F^2) was carried out with the SHELXL-97 program.[41] All non-hydrogen atoms were refined anisotropically and hydrogens were placed on idealized positions (–CH: U_{iso} = 1.2U_{eq}(C_{CH}), C–H: 1.00 Å; –CH_3: U_{iso} = 1.5U_{eq}-(C_{CH_3}), C–H: 0.98 Å; CH_{arom}: U_{iso} = 1.2U_{eq}(C_{arom}), C–H_{arom}: 0.95 Å). Crystallographic data are summarized in Table 2, bond lengths and angles in Table 1.

CCDC reference number 167084.

See http://www.rsc.org/suppdata/dt/b1/b102291c/ for crystallographic data in CIF or other electronic format.

Preparation of the *cis*-[$PtCl_2$(dmso)(oxadiazoline)] complexes

A suspension of *cis*-[$PtCl_2$(dmso)(PhCN)] (45 mg, 0.10 mmol) and the corresponding nitrone (0.11 mmol) in CH_2Cl_2 (2 ml) was stirred for 12 h at 56 °C (or 2 d at room temperature) and the progress of the reaction was monitored by TLC. After chromatography on SiO_2–CH_2Cl_2 and evaporation of the solvent, the product was obtained as a pale yellow oil that solidifies on standing overnight or upon addition of a few drops of diethyl ether.

***cis*-[$PtCl_2$(dmso){N=C(Ph)O–N(Me)–C(H)Ph}].** Yield 78%. Anal. calc. for $C_{17}H_{20}N_2Cl_2O_2PtS$: C, 35.06; H, 3.46; N, 4.81, S, 5.50. Found: C, 35.18; H, 3.44; N, 4.75; S, 5.50%. FAB$^+$-MS, *m*/*z*: 605 [M + Na]$^+$, 583 [M + H]$^+$, 546 [M − HCl]$^+$, 510 [M − 2HCl]$^+$. Mp 159 °C. TLC on SiO_2, R_f = 0.33 (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1630 s ν(C=N), 1126 s ν(S=O). ^{1}H NMR spectrum in $CDCl_3$, δ: 2.55 (s + d, $^3J_{PtH}$ 20.0 Hz, 3H) and 2.75 (s + d, $^3J_{PtH}$ 20.4 Hz, 3H) (dmso), 3.11 [s, C–N(*Me*)–O], 6.09 (s, br, 1H, N–C*H*–N), 7.50 (m, 3H), 7.61 (t, 7.8 Hz, 2H), 7.70 (t, 7.2 Hz, 1H), 7.86 (m, 2H) and 8.72 (d, 7.8 Hz, 2H) (two *Ph*). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: 43.5 ($^2J_{PtC}$ 52 Hz) and 43.6 ($^2J_{PtC}$ 52 Hz) (dmso), 46.5 [C–N-(*Me*)–O], 94.0 ($^2J_{PtC}$ 20 Hz, N–*C*H–N), 123.4, 129.7, 130.1 and 134.0 (=C*Ph*), 128.7 (*o*-Ph), 128.8 (*m*-Ph), 129.3 (*p*-Ph) and 136.2 (*ipso*-Ph) (CH*Ph*), 164.3 (C=N). ^{195}Pt NMR spectrum in $CDCl_3$, δ: −2957 (370 Hz).

***cis*-[$PtCl_2$(dmso){N=C(Ph)O–N(Me)–C(H)(C_6H_4Me)}].** Yield 83%. Anal. calc. for $C_{18}H_{22}N_2Cl_2O_2PtS$: C, 36.25; H, 3.72; N, 4.70, S, 5.36. Found: C, 36.49; H, 3.78; N, 4.42; S, 5.13%. FAB$^+$-MS, *m*/*z*: 619 [M + Na]$^+$, 597 [M + H]$^+$, 561 [M − HCl]$^+$, 524 [M − 2HCl]$^+$. Mp 141 °C. TLC on SiO_2, R_f = 0.37 (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1631 s ν(C=N), 1134 s ν(S=O). ^{1}H NMR spectrum in $CDCl_3$, δ: 2.40 (s, 3H, C_6H_4*Me*), 2.60 (s + d, $^3J_{PtH}$ 18.0 Hz, 3H) and 2.76 (s + d, $^3J_{PtH}$ 18.9 Hz, 3H) (dmso), 3.09 [s, C–N(*Me*)–O], 6.04 (s, br, 1H, N–C*H*–N), 7.31 (d, 8.1 Hz, 2H) and 7.74 (d, 7.8 Hz, 2H) (C_6H_4Me), 7.61 (t, 7.8 Hz, 2H), 7.71 (t, 7.8 Hz, 1H), 8.71 (d, 7.6 Hz, 2H) (*Ph*). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: 21.4 (C_6H_4*Me*), 43.5 ($^2J_{PtC}$ 52 Hz) and 43.6 ($^2J_{PtC}$ 50 Hz) (dmso), 46.3 [C–N(*Me*)–O], 94.0 ($^2J_{PtC}$ not observed, N–*C*H–N), 123.4, 129.4, 129.6 and 133.9 (=C*Ph*), 128.7, 129.3, 133.1 and 140.2 (C_6H_4Me), 164.2 (C=N). ^{195}Pt NMR spectrum in $CDCl_3$, δ: −2956 (370 Hz).

***cis*-[$PtCl_2$(dmso){N=C(Ph)O–N(Me)–C(H)(C_6H_4OMe)}].** Yield 80%. Anal. calc. for $C_{18}H_{22}N_2Cl_2O_3PtS$: C, 35.30; H, 3.62; N, 4.57, S, 5.22. Found: C, 35.47; H, 3.62; N, 4.48; S, 5.12%. FAB$^+$-MS, *m*/*z*: 635 [M + Na]$^+$, 613 [M + H]$^+$, 577 [M − HCl]$^+$, 540 [M − 2HCl]$^+$. Mp 142 °C. TLC on SiO_2, R_f = 0.35 (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1638 s ν(C=N), 1139 s ν(S=O). ^{1}H NMR spectrum in $CDCl_3$, δ: 2.68 (s + d, $^3J_{PtH}$ 17.0 Hz, 3H) and 2.76 (s + d, $^3J_{PtH}$ 14 Hz, 3H) (dmso), 3.09 [s, C–N(*Me*)–O], 3.86 (s, 3H, C_6H_4O*Me*), 6.03 (s, br, 1H, N–C*H*–N), 7.02 (d, 8.7 Hz, 2H) and 7.77 (d, 8.7 Hz, 2H) (C_6H_4OMe), 7.61 (t, 7.6 Hz, 2H), 7.72 (t, 7.8 Hz, 1H), 8.71 (d, 8.2 Hz, 2H) (*Ph*). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: 43.59 ($^2J_{PtC}$ 50 Hz) and 43.63 ($^2J_{PtC}$ 50 Hz) (dmso), 46.0 [C–N(*Me*)–O], 55.4 (C_6H_4O*Me*), 93.8 ($^2J_{PtC}$ not observed, N–*C*H–N), 123.4, 129.4, 131.1 and 133.9 (=C*Ph*), 114.0, 128.7, 127.9 and 160.9 (C_6H_4OMe), 164.2 (C=N). ^{195}Pt NMR spectrum in $CDCl_3$, δ: −2964 (380 Hz).

***cis*-[$PtCl_2$(dmso){N=C(Ph)O–N(CH_2Ph)–C(H)Ph}].** This compound contained about 10% of the corresponding *trans* isomer. Yield 71%. Anal. calc. for $C_{23}H_{24}N_2Cl_2O_2PtS$: C, 41.95; H, 3.67; N, 4.25, S, 4.86. Found: C, 42.32; H, 3.65; N, 4.19; S, 4.86%. FAB$^+$-MS, *m*/*z*: 681 [M + Na]$^+$, 659 [M + H]$^+$, 622 [M − HCl]$^+$, 586 [M − 2HCl]$^+$. TLC on SiO_2, R_f = 0.42 (major spot, *cis* isomer) and 0.52 (minor spot, *trans* isomer) (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1651 s ν(C=N), 1126 s ν(S=O). ^{1}H NMR spectrum in $CDCl_3$, δ: *cis* isomer: 2.54 (s + d, $^3J_{PtH}$ 19.0 Hz, 3H) and 2.78 (s + d, $^3J_{PtH}$ 20.1 Hz, 3H) (dmso), 4.27 (d, 13.2 Hz, 1H) and 4.51 (d, 13.2 Hz, 1H) (C*H*$_2$Ph), 6.34 (s, br, 1H, N–C*H*–N), 7.31–7.89 (m, 13H) and 8.70 (d, 7.0 Hz, 2H) (three Ph); *trans* isomer: 3.47 (s + d, $^3J_{PtH}$ 17.4 Hz, 6H), 4.30 (d, 13.2 Hz, 1H) and 4.50 (d, 13.2 Hz, 1H) (C*H*$_2$Ph), 6.23 (s, br, 1H, N–C*H*–N), (signals of the phenyl groups are overlapped by those of the major isomer). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: *cis* isomer: 43.5 ($^2J_{PtC}$ 51 Hz) and 43.6 ($^2J_{PtC}$ 51 Hz) (dmso), 63.3 (*C*H$_2$Ph), 91.7 ($^2J_{PtH}$ not observed, N–*C*H–N), 128.68, 128.71, 128.76, 129.29, 129.50 and 129.52 ($CH_{o,m}$), 129.86, 129.90 and 134.0 (CH_p), 133.5, 134.5 and 134.9 (C_{ipso}) (three Ph), 164.4 (C=N); *trans* isomer: 44.4 ($^2J_{PtC}$ not observed due to low signal intensity) (dmso), 62.3 (*C*H$_2$Ph), 90.6 ($^2J_{PtH}$ not observed, N–*C*H–N), signals of the phenyl groups not assigned due to overlap with the signals

of the major isomer, C=N not detected. ^{195}Pt NMR spectrum in $CDCl_3$, δ: *cis* isomer: −2957 (370 Hz), *trans* isomer: −3087 (380 Hz).

Preparation of *cis*-[$PtCl_2$(PhMeSO)(PhCN)]

PhMeSO (106 mg, 0.76 mmol) was dissolved in water (1 ml) and added dropwise to a stirred aqueous solution (5 ml) of K_2PtCl_4 (300 mg, 0.72 mmol). The reaction mixture was left at room temperature for 12 h, after which time a small amount of pale yellow solid [$PtCl_2$(PhMeSO)$_2$] was filtered off. PhCN (78 μl, 0.76 mmol) was added to the filtrate and the mixture left standing at room temperature for 1 week. The pale yellow solid formed was collected by filtration, washed with water and dried *in vacuo*.

Yield 56%. Anal. calc. for $C_{14}H_{13}NCl_2OPtS$: C, 33.02; H, 2.57; N, 2.75, S, 6.28. Found: C, 33.24; H, 2.47; N, 2.72; S, 6.29%. FAB$^+$-MS, *m*/*z*: 532 [M + Na]$^+$, 509 [M]$^+$, 473 [M − HCl]$^+$, 437 [M − 2HCl]$^+$. TLC on SiO_2, R_f = 0.21 (eluent CH_2Cl_2), 0.58 (eluent CH_2Cl_2–diethyl ether 9 : 1 v : v). IR spectrum (selected bands), cm^{-1}: 2284 m ν(C≡N), 1148 s ν(S=O). ^{1}H NMR spectrum in $CDCl_3$, δ: 3.65 (s + d, $^3J_{PtH}$ 18.9 Hz, 3H, Ph*Me*SO), 7.54 (t, 7.8 Hz, 2H), 7.71 (d, 7.5 Hz, 2H) and 7.76 (t, 7.8 Hz, 1H) (*Ph*CN), 7.65 (m, 3H) and 8.18 (m, 2H) (*Ph*MeSO). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: 45.5 ($^2J_{PtC}$ 62.5 Hz, Ph*Me*SO), 108,9 (*ipso*-PhCN), 114.8 (C≡N), 125.7 and 129.5 (*o*- and *m*-*Ph*MeSO), 129.6 and 133.37 (*o*- and *m*-PhCN), 133.40 (*p*-*Ph*MeSO), 135.3 (*p*-PhCN), 141.9 (*ipso*-*Ph*MeSO). ^{195}Pt NMR spectrum in $CDCl_3$, δ: −3007 (590 Hz).

Preparation of the [$PtCl_2$(PhMeSO)(oxadiazoline)] complexes

A suspension of *cis*-[$PtCl_2$(PhMeSO)(PhCN)] (51 mg, 0.10 mmol) and the corresponding nitrone (0.11 mmol) in CH_2Cl_2 (2 ml) was stirred for 12 h at 56 °C or 2 d at room temperature and completion of the reaction was confirmed by TLC. After chromatography on SiO_2–CH_2Cl_2, the individual products were recrystallized by slow evaporation of a CH_2Cl_2–diethyl ether solution and obtained as pale yellow solids.

***cis*-[$PtCl_2$(PhMeSO){N=C(Ph)O–N(Me)–C(H)Ph}].** Two diastereoisomers (80% : 20%). Yield 71%. Anal. calc. for $C_{22}H_{22}N_2Cl_2O_2PtS$: C, 41.00; H, 3.44; N, 4.35, S, 4.96. Found: C, 41.13; H, 3.46; N, 4.28; S, 4.88%. FAB$^+$-MS, *m*/*z*: 667 [M + Na]$^+$, 644 [M]$^+$, 608 [M − HCl]$^+$, 572 [M − 2HCl]$^+$. TLC on SiO_2, R_f = 0.40 (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1622 s ν(C=N), 1138 s ν(S=O). ^{1}H NMR spectrum in $CDCl_3$, δ: major isomer: 3.06 and 3.07 [two s, 3H each, Ph*Me*SO and C–N(*Me*)–O], 6.03 (s, br, 1H, N–C*H*–N), 6.99 (m, 2H), 7.32 (m, 2H), 7.47 (m, 1H), 7.53–7.77 (m, 8H) and 8.89 (d, 7.0 Hz, 2H) (three Ph); minor isomer: 2.95 and 3.12 [two s, 3H each, Ph*Me*SO and C–N(*Me*)–O], 6.19 (s, br, 1H, N–C*H*–N), 8.06 (d, 7.2 Hz, 2H) and 8.49 (d, 7.5 Hz, 2H), (other signals not assigned due to overlap with signals of the major isomer). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: major isomer: 46.1 and 46.4 [Ph*Me*SO and C–N(*Me*)–O], 94.1 (N–*C*H–N), 125.9, 128.3, 128.6, 128.7, 128.8 and 129.3 ($CH_{o,m}$), 129.7, 132.4, 133.9 (CH_p), 133.4, 134.9 and 141.5 (C_{ipso}), 164.5 (C=N); minor isomer: 45.1 and 46.2 [Ph*Me*SO and C–N(*Me*)–O], 94.0 (N–*C*H–N), (other signals not assigned due to overlap with signals of the major isomer). ^{195}Pt NMR spectrum in $CDCl_3$, δ: −2975 (370 Hz) (major isomer, 80%) and −2930 (400 Hz) (minor isomer, 20%).

***cis*-[$PtCl_2$(PhMeSO){N=C(Ph)O–N(Me)–C(H)(C_6H_4Me)}].** Two diastereoisomers (70% : 30%). Yield 68%. Anal. calc. for $C_{23}H_{24}N_2Cl_2O_2PtS$: C, 41.95; H, 3.67; N, 4.25, S, 4.86. Found: C, 42.01; H, 3.63; N, 4.18; S, 4.78%. TLC on SiO_2, R_f = 0.39 (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1624 s ν(C=N), 1136 s ν(S=O). ^{1}H NMR spectrum in $CDCl_3$, δ: major isomer: 2.07 (s, 3H, C_6H_4*Me*), 3.00 and 3.02 [two s, 3H each, Ph*Me*SO and C–N(*Me*)–O], 5.94 (s, br, 1H, N–C*H*–N), 6.70 (d, 8.0 Hz, 2H), 7.25–7.75 (m, 10H) and 8.85 (d, 7.9 Hz, 2H) (2 Ph and C_6H_4Me); minor isomer: 2.40 (s, 3H, C_6H_4*Me*), 2.95 and 3.04 [two s, 3H each, Ph*Me*SO and C–N(*Me*)–O], 6.09 (s, br, 1H, N–C*H*–N), 7.16 (d, 7.8 Hz, 2H), 7.86 (d, 7.8 Hz, 2H) and 8.45 (d, 8.1 Hz, 2H) (2 Ph and C_6H_4Me, other signals not assigned due to overlap with signals of the major isomer). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: major isomer: 21.3 (C_6H_4-*Me*), 45.9 and 46.5 [Ph*Me*SO and C–N(*Me*)–O], 94.0 (N–*C*H–N), 126.0, 128.60, 128.64, 128.70, 129.0, 129.3 ($CH_{o,m}$), 132.3, 133.9 (CH_p), 123.7, 132.1, 139.4 and 141.4 (C_{ipso}), 164.3 (C=N); minor isomer: 21.4 (C_6H_4*Me*), 45.0 and 45.8 [Ph*Me*SO and C–N(*Me*)–O], 93.9 (N–*C*H–N), 125.3, 128.3, 128.5, 129.1, 129.2, 129.8 ($CH_{o,m}$), 132.0, 133.5 (CH_p), 122.4 132.6, 140.0 and 142.0 (C_{ipso}), 164.2 (C=N). ^{195}Pt NMR spectrum in $CDCl_3$, δ: −2979 (400 Hz) (major isomer, 70%) and −2928 (400 Hz) (minor isomer, 30%).

***cis*-[$PtCl_2$(PhMeSO){N=C(Ph)O–N(Me)–C(H)(C_6H_4OMe)}].** Two diastereoisomers (65% : 35%). Yield 70%. Anal. calc. for $C_{23}H_{24}N_2Cl_2O_3PtS$: C, 40.96; H, 3.59; N, 4.15, S, 4.74. Found: C, 41.20; H, 3.58; N, 4.02; S, 4.67%. TLC on SiO_2, R_f = 0.35 (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1628 s ν(C=N), 1142 s ν(S=O). ^{1}H NMR spectrum in $CDCl_3$, δ: major isomer: 3.00 and 3.02 [two s, 3H each, Ph*Me*SO and C–N(*Me*)–O], 3.60 (s, 3H, C_6H_4O*Me*), 5.93 (s, br, 1H, N–C*H*–N), 6.43 (d, 8.4 Hz, 2H), 7.14–7.70 (m, 10H) and 8.88 (d, 7.2 Hz, 2H) (2 Ph and C_6H_4OMe); minor isomer: 2.99 and 3.04 [two s, 3H each, Ph*Me*SO and C–N(*Me*)–O], 3.83 (s, 3H, C_6H_4O*Me*), 6.05 (s, br, 1H, N–C*H*–N), 7.05 (d, 8.0 Hz, 2H), 7.92 (d, 8.0 Hz, 2H), 8.44 (d, 7.5 Hz, 2H) (2 Ph and C_6H_4OMe, other signals not assigned due to overlap with signals of the major isomer). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: major isomer: 45.8 and 46.4 [Ph*Me*SO and C–N(*Me*)–O], 54.8 (O*Me*), 93.9 (N–*C*H–N), 113.6, 125.9, 128.58, 128.63, 129.3, 130.2 ($CH_{o,m}$), 132.4, 133.8 (CH_p), 123.6, 126.9, 141.4 and 160.3 (C_{ipso}), 164.2 (C=N); minor isomer: 45.2 and 45.5 [Ph*Me*SO and C–N(*Me*)–O], 55.5 (O*Me*), 93.9 (N–*C*H–N), 113.8, 125.2, 128.3, 128.58, 129.3, 131.9 ($CH_{o,m}$), 132.0, 133.5 (CH_p), 122.4, 127.4, 142.0 and 160.9 (C_{ipso}), 164.5 (C=N). ^{195}Pt NMR spectrum in $CDCl_3$, δ: −2982 (370 Hz) (major isomer, 65%) and −2930 (400 Hz) (minor isomer, 35%).

Release of the Δ^4-1,2,4-oxadiazolines from the complexes

To a solution of the corresponding *cis*-[$PtCl_2$(sulfoxide)-(oxadiazoline)] complex (0.1 mmol) in 2 ml of chloroform an excess of ethane-1,2-diamine (30 mg, 0.5 mmol) was added and the reaction mixture stirred for two hours at room temperature. During this time, the initially pale yellow solution turned practically colourless and a white precipitate was formed. Extraction of the reaction mixture with 0.5 ml of water gives a pale yellow aqueous phase and a colourless organic layer that was separated, washed with water (2 × 0.5 ml to remove dmso, 4 × 0.5 ml to remove PhMeSO) and dried with Na_2SO_4. Evaporation of the solvent afforded the individual Δ^4-1,2,4-oxadiazolines as colourless oils. Further purification can be achieved by chromatography on silica gel with CH_2Cl_2 as eluent.

{N=C(Ph)O–N(Me)–C(H)(Ph)} (ref. 42). Yield 88%. TLC on SiO_2, R_f = 0.46 (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1660 s ν(C=N). ^{1}H NMR spectrum in $CDCl_3$, δ: 2.99 [s, C–N(*Me*)–O], 5.77 (s, br, 1H, N–C*H*–N), 7.24–7.52 (m, 8H) and 8.00 ("d", 7.8 Hz, 2H) (two *Ph*). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: 46.7 [br, C–N(*Me*)–O], 93.7 (br, N–*C*H–N), 125.5, 126.5 (br), 128.2, 128.3, 128.41, 128.44, 131.8 and 139.6 (br) (two *Ph*), 160.5 (br, C=N).

{N=C(Ph)O–N(CH$_2$Ph)–C(H)(Ph)}. Yield 74%. TLC on SiO_2, R_f = 0.72 (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1667 s ν(C=N). ^{1}H NMR spectrum in $CDCl_3$, δ: 4.10 (d, 12.9 Hz, 1H) and 4.40 (d, 12.2 Hz, 1H) (CH_2Ph), 6.01 (s, br, 1H, N–CH–N), 7.26–7.50 (m, 12H), 7.55 (t, 7.5 Hz, 1H) and 8.00 (d, 7.3 Hz, 2H) (three Ph). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: 63.1 (CH$_2$Ph), 90.6 (N–CH–N), 126.4 (br), 128.33, 128.42, 128.46, 128.54 and 129.5 (CH$_{o,m}$), 127.8, 128.1 and 131.9 (CH$_p$), 133.8, 135.2 and 135.3 (C$_{ipso}$) (three Ph), 161.6 (C=N).

{N=C(Ph)O–N(Me)–C(H)(C$_6$H$_4$Me)}. Yield 84%. TLC on SiO_2, R_f = 0.54 (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1666 s ν(C=N). ^{1}H NMR spectrum in $CDCl_3$, δ: 2.34 (s, 3H, C$_6$H$_4$*Me*), 2.96 [s, C–N(*Me*)–O], 5.75 (s, br, 1H, N–CH–N), 7.17 (d, 7.8 Hz, 2H) and 7.34 (d, 8.1 Hz, 2H) (C$_6H_4$Me), 7.45 (t, 7.2 Hz, 2H), 7.53 (t, 7.5 Hz, 1H) and 7.99 (d, 7.0 Hz, 2H) (*Ph*). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: 21.1 (C$_6$H$_4$*Me*), 46.9 [br, C–N(*Me*)–O], 93.8 (br, N–CH–N), 126.5 (br), 128.4, 128.5, 128.6, 129.2, 131.9, 136.9 (br) and 138.1 (Ph and C_6H$_4$Me), 160.1 (br, C=N).

{N=C(Ph)O–N(Me)–C(H)(C$_6$H$_4$OMe)}. Yield 91%. TLC on SiO_2, R_f = 0.49 (eluent CH_2Cl_2). IR spectrum (selected bands), cm^{-1}: 1662 s ν(C=N). ^{1}H NMR spectrum in $CDCl_3$, δ: 2.97 [s, C–N(*Me*)–O], 3.80 (s, 3H, C$_6$H$_4$O*Me*), 5.74 (s, br, 1H, N–CH–N), 6.91 (d, 8.7 Hz, 2H) and 7.39 (d, 8.7 Hz, 2H) (C$_6H_4$OMe), 7.47 (t, 7.8 Hz, 2H), 7.54 (t, 7.8 Hz, 1H) and 8.01 (d, 7.8 Hz, 2H) (*Ph*). ^{13}C{^{1}H} NMR spectrum in $CDCl_3$, δ: 46.7 [br, C–N(*Me*)–O], 55.2 (C$_6$H$_4$O*Me*), 93.5 (br, N–CH–N), 113.9, 125.6, 127.8 (br), 128.44, 128.48, 128.52, 131.9 and 159.7 (Ph and C_6H$_4$OMe), 160.5 (C=N).

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