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Highly Stereoselective 1,3-Dipolar Cycloaddition of Nitrones to (Nitrile)$_2$Pt^{II} Species Furnishing Diastereomerically Pure 2,3-Dihydro-1,2,4-oxadiazole Ligands

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Diastereomerically pure platinum(II) complexes **4**−**9** bearing tetrahydro-5,8-methanocyclohexa-[3′,2′:4,5][1,3]oxazolo[3,2-*b*][1,2,4]oxadiazole ligands were generated under mild conditions (CH_2Cl_2, 20−25 °C, 24 h) by an intermolecular Pt^{II}-mediated 1,3-dipolar cycloaddition between enantiomerically pure camphor-derived oxazoline-*N*-oxides and the coordinated nitriles in the complexes *trans*-[$PtCl_2$(R′CN)$_2$] (R′ = Et, Ph, NMe_2). These species were characterized by elemental analyses (C, H, N), high-resolution ESI$^+$-MS, IR, ^{1}H and ^{13}C NMR spectroscopies, and also X-ray diffraction (for **5**, **7**, **8**·$CHCl_3$, and **9**·Me_2CO). Free heterocycles **10**−**13** were liberated as single stereoisomers from the (2,3-dihydro-1,2,4-oxadiazole)$_2$Pt^{II} complexes (R = Et, Ph) by treatment with excess NaCN and were characterized by high-resolution ESI$^+$-MS and ^{1}H and ^{13}C NMR spectroscopies.

Introduction

1,3-Dipolar cycloaddition (1,3-DCA) of nitrones represents an extensively studied method for synthesis of five-membered N,O-containing heterocycles.[1−3] As far as the stereoselectivity of 1,3-DCA of nitrones to various dipolarophiles is concerned, this cycloaddition leads to the construction of up to three contiguous asymmetric carbon centers (e.g., in reaction with alkenes[2−7]), and the stereocontrol in these processes can be achieved by the use of chiral catalysts (such as Brønsted[8,9] or Lewis acids[5,10−18]) or stoichiometric chiral auxiliaries[12,19,20] that are attached either to the dipole or to the dipolarophile. Alternatively, the stereoselectivity of the cycloaddition can be reached by use asymmetric enantiomerically pure starting material(s).[9,27]

In contrast to reactions of nitrones with alkenes,[2−7] their 1,3-DCA to nitriles is much less explored, which relates to a poor dipolarophilicity of RCN species.[21] As a consequence, in metal-free organic chemistry very few examples of 1,3-DCA of nitrones to a restricted range of electron-deficient nitriles are known.[22−27] Substantial progress in this area was achieved in the past decade by application of metal centers in high oxidation states as extremely strong activators of RCN

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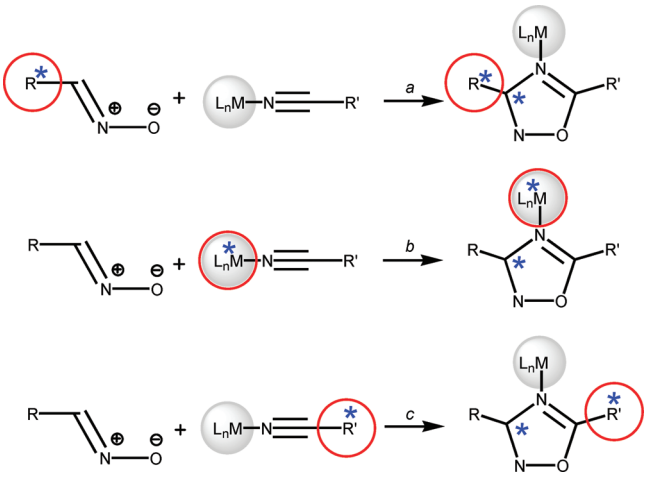
substrates toward CA of both allyl- and propargyl/allenyl anion type dipoles.[21,28−40]

The use of a metal, such as platinum(II) and -(IV), for activation of RCN substrates resulted, in some instances, in rate enhancement of the known 1,3-DCA reactions,[31,32] but—what is the most attractive—also allows the conductance of such cycloadditions, which are not yet feasible for metal-free organic chemistry, e.g., 1,3-DCA of electron-deficient nitrones to electron-enriched nitriles.[28,31,33,41] Thus, we recently found that the platinum(II)-mediated DCA of cyclic nitrones to metal-bound RCN substrates proceeds smoothly and opens access to new types of fused heterocyclic systems such as 3a,4,5,6-tetrahydro-[1,3]oxazolo[3,2-*b*][1,2,4]oxadiazoles[33] and 3a,4,5,6-tetrahydro-[1,3]imidazo[1,2-*b*][1,2,4]oxadiazoles;[28] the latter species exhibit substantial stability when coordinated, but undergo retro-cycloaddition, being liberated from the metal center.

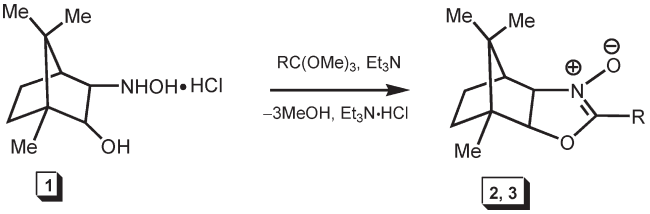
In the nitrone−nitrile DCA, a new asymmetric carbon center is formed (Scheme 1), and at least two strategies can be applied to achieve stereoselectivity of these reactions: (i) stereocontrol could be provided by a chiral nitrone dipole (Scheme 1, *a*),[23] (ii) stereocontrol could be provided by a dipolarophile, either when a metal complex bears both achiral nitrile and chiral supporting ligands (*b*) or when a nitrile having chiral substituent is employed (*c*).[27,33,42]

Currently, only two reports related to the stereoselectivity of the metal-mediated nitrone−nitrile DCA are known from the literature.[33,42] The first[42] describes the Pt^{II}-mediated enantioselective formation of 2,3-dihydro-1,2,4-oxadiazole, when the metal center, having the chiral sulfoxide (*S*)-PhMeS*O (ee 79%) ligand in the *cis* position to the reacting RCN, is used as a chiral auxiliary group. This asymmetric induction approach (see Scheme 1, *b*) provided 30−70% de, while decoordination of 2,3-dihydro-1,2,4-oxadiazoles formed in DCA allows the generation of the *S*-enantiomers with ee up to 70%.[42] The second work[33] reports on a stereocontrol in a Pt^{II}-mediated DCA imposed by a bulky chiral ligand in *trans* position to a coordinated nitrile substrate. This reaction also belongs to type *b* (Scheme 1); it occurred diastereoselectively but afforded mixtures of enantiomers after decoordination of heterocycles.

Scheme 1. Strategies of Stereoselective Metal-Mediated Cycloaddition of Nitrones to Nitriles



Scheme 2. Synthetic Route to Oxazoline-*N*-oxides 2 (R = Me) and 3 (R = Et)



In this work, we explored route *a* (Scheme 1), by application of an enantiomerically pure asymmetric nitrone, to provide the stereocontrol of the cycloaddition. We now report on the first example of highly stereoselective metal-mediated generation of 2,3-dihydro-1,2,4-oxadiazoles. The scenario of this work was the following: first, we improved synthesis of the known chiral dipole that is, in accord with IUPAC nomenclature,[43] (3a*S*,4*R*,7*S*,7a*R*)-2-R-4,8,8-trimethyl-3a,7a-dihydro-4,7-methanocyclohexa[3,2-*d*][1,3]oxazol-*N*-oxide) (**2** and **3** in Scheme 2). Second, we performed highly stereoselective DCA of this dipole to ligated RCN species at a platinum(II) center and characterized the diastereomerically pure (2,3-dihydro-1,2,4-oxadiazole)$_2Pt^{II}$ complexes. Eventually, third, we liberated the heterocyclic ligands, by the reaction with NaCN, to furnish enantiomerically pure dihydrooxadiazoles, i.e., IUPAC name[43] {(3a*S*,4a*S*,5*R*,8*S*,8a*R*)-2-R′-3a-R-5,10,10-trimethyl}-3a,4a,8a,9-tetrahydro-5,8-methanocyclohexa[3′,2′:4,5][1,3]oxazolo[3,2-*b*][1,2,4]oxadiazole species. All these data are consistently reported in this article.

Results and Discussion

Pt^{II}-Mediated 1,3-Dipolar Cycloaddition. In terms of orbital interactions, nitrone−nitrile 1,3-DCA reactions are classified as interaction with normal or borderline electron demand,[44−49]

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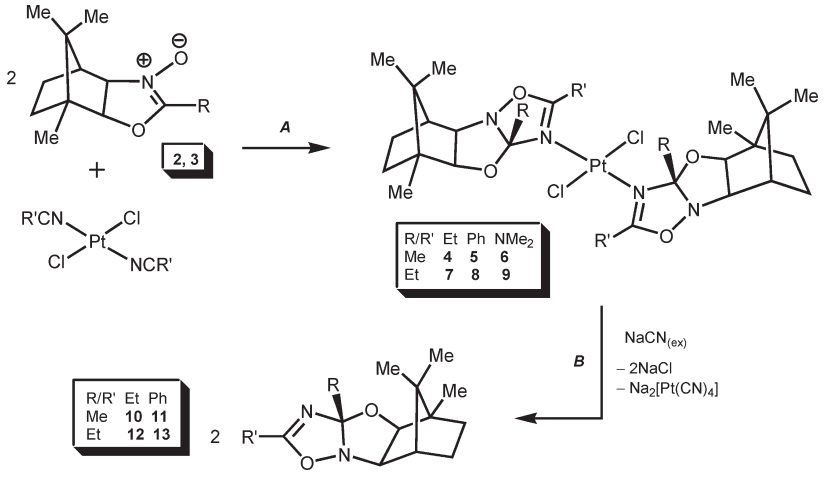
Scheme 3. Pt^{II}-Mediated Cycloaddition and Liberation of the Heterocycles



when the HOMO of the dipole interacts with the LUMO of the dipolarophile. By coordination, the $LUMO_{nitrile}$ energy is significantly lowered compared to that of the uncoordinated RCN, giving rise to a more favorable $HOMO_{nitrone}-LUMO_{nitrile}$ interaction, leading to an increase of the reaction rate with the nitrone.[46−49] In turn, coordination of nitrone leads to increasing of the $HOMO_{nitrone}-LUMO_{nitrile}$ gap, disfavoring DCA. It was previously demonstrated that a Pt^{II} center provides a sufficient activation of ligated nitriles to perform the reaction with oxazoline *N*-oxides and to make it selective, while the use of a Pt^{IV} center in 1,3-DCA leads to loss of the selectivity and the formation of a broad mixture of products.[33] Hence, for this study we addressed a Pt^{II} center for activation of nitriles in DCA with camphor-derived oxazoline-*N*-oxides **2** and **3** (Scheme 2) obtained *in situ* from (+)-3-(hydroxylamino)isoborneol hydrochloride **1** (for an improved synthesis of enantiomericaly pure 1,3-dipoles **2** and **3** see the Supporting Information).

1,3-DCA between **2** or **3** and *trans*-$[PtCl_2(NCR')_2]$ (R′ = Et, Ph, NMe_2) proceeds for 1 day at room temperature. Characterization of the products (see next section) revealed that reactions of the coordinated NCR′ with the oxazoline *N*-oxides afforded (dihydrooxazolo-1,2,4-oxadiazole)$_2Pt^{II}$ complexes **4**−**9** (Scheme 3, route *A*) in ca. 92−95% NMR yields. These species were purified by column chromatography on SiO_2 and isolated in 66−90% yields.

The cycloaddition described above is Pt^{II}-mediated. In a separate experiment, it was proved that among the studied ligands the most electron-deficient nitrile, i.e., PhCN, in $CDCl_3$ in the absence of the metal center does not react with the dipoles at 50 °C for 1 day, and only gradual degradation of the oxazoline *N*-oxides was observed under applied conditions.

Characterization of (Dihydrooxazolo-1,2,4-oxadiazole)Pt^{II} Complexes. Complexes **4**−**9** were isolated as yellow solids and characterized by elemental analyses (C, H, N), high-resolution electrospray mass spectrometry, IR, ^1H and $^{13}C\{^1H\}$ NMR spectroscopies, and also X-ray diffraction (for **5**, **7**, **8**·$CHCl_3$, and **9**·Me_2CO). The complexes gave satisfactory microanalyses and the expected fragmentation/isotopic pattern in ESI^+-MS; the typical ions that were detected are $[M]^+$ and $[M + NH_4]^+$. In the IR spectra, the ν(C≡N) stretching vibrations at ca. 2300 cm^{-1} are not displayed, but the intense band that was assigned to the C═N stretch of the 2,3-dihydro-1,2,4-oxadiazole ring was observed in the 1632−1669 cm^{-1} range.

The ^1H NMR spectra of **4**−**9** in $CDCl_3$ differ from the corresponding spectra of the starting materials and give evidence that the reaction between each of the coordinated nitriles and an oxazoline *N*-oxide proceeds in a 1:1 molar ratio. In the $^{13}C\{^1H\}$ NMR spectra of **4**−**9**, resonances due to C═N (158.8−172.8 ppm) and C^{3a} (118.3−122.8 ppm) were recognized. Both the ^1H and the ^{13}C NMR spectra display only one set of signals, thus providing evidence favoring the availability of only one diastereomer and the absence of the *meso*-form.

Compounds **5**, **7**, **8**·$CHCl_3$, and **9**·Me_2CO (Figure 1 and Figures S1−S3; for the latter see Supporting Information) have square-planar geometries and exhibit a *trans* configuration. The Pt−N bond lengths [2.002(2)−2.026(2) Å] (Table 2) in the complexes are typical for (imine)Pt^{II} species and similar to those [2.011(2)−2.0164(12) Å] in the related *trans*-(5,6-dihydro-3a*H*-[1,3]oxazolo[3,2-*b*]-[1,2,4]oxadiazole)$_2Pt^{II}$ compounds;[33] the Pt−Cl distances [2.2945(9)−2.3121(6) Å] fall in the typical range for *trans*-$Pt^{II}Cl_2$ moieties.[28,32,33,50,51]

The bond lengths N(1)−C(2) and N(3)−C(21) [1.280(4)−1.304(3) Å] agree well with the average value for the N═C double bond,[52] while N(2)−C(8) and N(4)−C(28) [1.483(3)−1.497(3) Å] are typical of single C−N bonds.[52] In all four structures, both asymmetric atoms C^{3a} in the heterocyclic ligands have the same absolute configuration (*S*). The identification of this configuration is consistent with our ideas on stereochemistry of this reaction path. The latter are based on configuration of the starting oxazoline-*N*-oxide and additionally supported by detection of only one set of signals in the NMR spectra.

Liberation of the Heterocycles and Their Characterization. Several approaches were previously developed for the liberation of imines and N-bonded heterocycles from their Pt^{II} complexes. Thus, our group[32,50,53−56] and Michelin et al.[57−59] observed that

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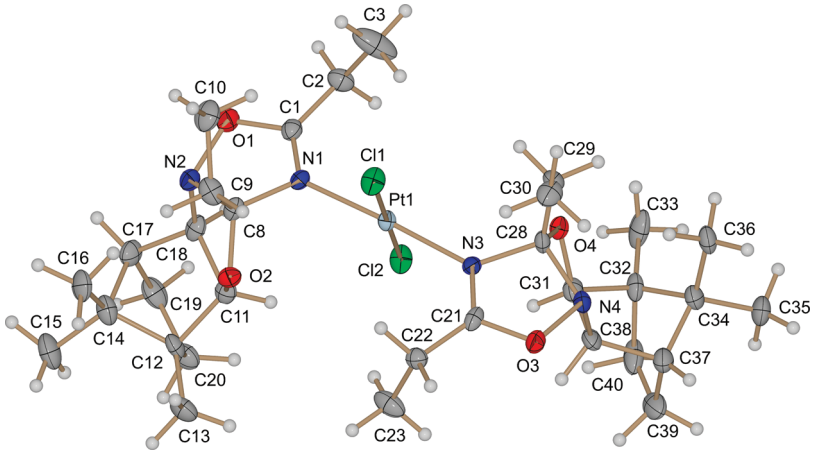

Figure 1. View of **7** with the atom-numbering scheme. Thermal ellipsoids are drawn at the 50% probability level.

the liberation of coordinated imines is efficient when (imine)Pt^{II} complexes are treated with bidentate diphosphines to give quantitative yield of the imine in solution and the solid [Pt(diphosphine)$_2$]Cl_2. In another approach, the heterocyclic ligands in the complexes [$PtCl_2$(dihydro-1,2,4-oxadiazole)$_2$] were liberated by treatment with an excess of chelating diamines.[33,42]

In this work, ligand liberation was attempted with $Ph_2PCH_2CH_2PPh$ (dppe; 2−4 equiv) in $CHCl_3$ and $NH_2CH_2CH_2NH_2$ (en; 20-fold excess) in CH_2Cl_2. We observed that the heterocycles are so strongly bound to the metal center that under mild conditions (room temperature, 2−4 equiv dppe) a significant amount of the coordinated heterocycle remains in the reaction mixture after 5 days, and under more drastic conditions (4 equiv dppe, 3 days at 40 °C, or 40 equiv en, 2 days at 35 °C) a broad mixture of products was formed due to ligand decoordination and its further decomposition.

However, it was recently reported that the cyanides could be applied for decoordination of some chelated phosphine ligands, and this observation indicates that alkali metal cyanide species are highly potent reactants for the displacement of strongly bound ligands at Pt^{II} centers.[60] In accord with this assumption, we observed that treatment of **4**, **5**, **7**, and **8** complexes with NaCN (8 equiv, in CD_2Cl_2/MeOD-d_4, 35 °C) leads to the quantitative generation of the free 2,3-dihydro-1,2,4-oxadiazoles (Scheme 3, route B). Completeness of the reaction was monitored by ^{1}H NMR, and almost quantitative conversion was observed after 4−6 h (for complexes **4** and **7**) and 18 h (for **5** and **8**). Heterocycles **10**−**13** were separated as colorless oily residues after evaporation of the solvent followed by extraction with CH_2Cl_2 and removal of the latter *in vacuo* at 20−25 °C. Dihydrooxazolo-1,2,4-oxadiazoles **10** and **12** were obtained with 98% purity, while **11** and **13** were contaminated with some other yet unidentified byproduct (5−7% based on ^{1}H NMR integration), which were formed in the course of ligand liberation due to lower stability of heterocycles bearing an electron-withdrawing substituent (Ph).[61]

All heterocycles that were liberated were characterized by ^{1}H and $^{13}C\{^1H\}$ NMR and high-resolution ESI^+-MS. In the ^{1}H and $^{13}C\{^1H\}$ NMR spectra, heterocycles **10**−**13** exhibit one set of signals. A characteristic feature of the ^{1}H NMR spectra is the availability of the signal from the CH proton at 3.81−3.90 ppm, which is high-field shifted (0.7−0.8 ppm) relative to the corresponding signals of the complexed heterocycles. In **10** and **12**, the signals of the methylene group from the N=CEt fragment emerge at 2.34 and 2.35 ppm as clearly resolved quartets (in **4** and **7**, the signals from these CH_2's appear at 3.03−3.26 ppm), and *o*-Ph protons from **11** and **13** resonate at 7.98 ppm (at 9.47 and 9.39 ppm in **5** and **8**, respectively). In the $^{13}C\{^1H\}$ NMR spectra of **10**−**13**, resonances due to C=N (162.7−167.9 ppm) and C^{3a} (121.5−124.0 ppm) were recognized. The typical ion that was detected in the ESI^+-MS is $[M + H]^+$.

Our substitution experiments indicate that in complexes **6** and **9** the heterocycles are so strongly ligated to the metal centers that the liberation of the dihydrooxazolo-1,2,4-oxadiazoles in preparative scale could not be achieved even at prolonged heating in a CD_2Cl_2/MeOD-d_4 mixture (5 days, 35 °C) with a 40-fold molar excess of NaCN. Under these conditions the starting complexes were detected by ^{1}H NMR, while some new signals (at 3.8 ppm) have less than 3% intensity. In the ESI^+-MS of the reaction mixtures, the molecular ions of **6** and **9** were detected as the most intensive signals, while a much less intensive peak at 280.1988 (calcd 280.2025; $[M + H]^+$ of the free heterocycle) was observed only for the reaction of **6** with NaCN.

Final Remarks

In metal-free organic chemistry, only one paper[27] provides a brief discussion on the stereoselective cycloadditions of an asymmetric nitrone to a nitrile functionality. The examples reported are restricted to exclusively electron-deficient nitriles, and in addition, the cycloaddition studied requires harsh reaction conditions. In this work, we employed the metal center for substantial activation of the R′CN substrates (both electron-enriched and electron-deficient) toward 1,3-DCA with nitrones, and we also provided the stereocontrol of the cycloaddition by application of the enatiomerically pure chiral dipole. As a result, we developed the high-yield stereoselective synthesis performed under mild conditions of the diastereomerically pure Pt^{II} complexes bearing the 2,3-dihydro-1,2,4-oxadiazoles. The reaction has a general character, and it was successfully employed to

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activated (with acceptor group, R′ = Ph) and nonactivated (with donor group, R′ = Et) nitriles and even to the so-called push−pull R′CN species (R′ = NMe_2). Despite that the heterocycles are strongly bound to the platinum(II) center, in four cases we succeeded in their liberation upon treatment of the complexes with NaCN to give the metal-free enatiomerically pure 2,3-dihydro-1,2,4-oxadiazoles.

The presence of the soft and kinetically inert platinum(II) metal center, when the nitrone reacts selectively with the dipolarophile and does not affect the dipole, does appear key to the success of these CAs. The skeptical reader, however, may feel some dissatisfaction with the use of the Pt starting material, which makes the suggested synthesis of enantiomerically pure 2,3-dihydro-1,2,4-oxadiazoles rather expensive. We still believe that the Pt^{II}-mediated CA is so far the only route to this type of heterocycles, and for a while one should be satisfied with achieving these compounds by any means. In addition, the conventional recycling[62] of platinum might strongly reduce all expenses associated with these synthetic transformations.

Results obtained in this work could be considered from at least two perspectives. In the narrow sense, we developed a facile method to diastereomerically pure $[PtCl_2L_2]$ complexes bearing 2,3-dihydro-1,2,4-oxadiazoles. Given that one can envisage the preparation of a spectrum of chiral nitrones (or, on the contrary, chiral nitriles), it follows that the Pt^{II}-mediated cycloaddition reactions could provide efficient routes to diastereomerically pure ligand systems. Previously, a relevant example of diastereomericaly pure $(imine)_2Pt^{II}$ complex generated from $(nitrile)_2Pt^{II}$ species via nucleophilic addition of chiral camphor-derived oxime was reported.[63]

Special attention should be drawn to the fact that platinum(II) complexes with 2,3-dihydro-1,2,4-oxadiazoles, where the heterocycles are mixtures of stereomers, are of biological importance, exhibiting antitumor properties.[64,65] Furthermore, we found a route for the decoordination of tetrahydro-5,8-methanocyclohexa[3′,2′:4,5][1,3]oxazolo-[3,2-*b*][1,2,4]oxadiazoles to form a single enantiomer. One should mention that the chemistry of 2,3-dihydro-1,2,4-oxadiazoles is very little developed and their properties, including biological activity, are unknown. We hope that our method for the stereoselective generation of these heterocyclic systems will contribute to the development of this field of chemistry of heterocycles.

In the wide sense, the described method, which utilizes a reaction between an enantiomerically pure reactant and metal-activated substrate followed by decoordination of newly formed ligands, could be efficiently used for generation of other diastereomerically or enantiomerically pure systems.

Experimental Section

Materials and Instruments. The orthoesters $RC(OEt)_3$ (R = Me, Et) and solvents were obtained from commercial sources and used as received. (+)-3-(Hydroxylamino)isoborneol **1** was synthesized by a modified literature method (see Supporting Information).[66,67] The complexes *trans*-$[PtCl_2(R'CN)_2]$ (R′ = Et,[68] Ph,[69,70] NMe_2[71]) were prepared in accord with the published methods.

Elemental analyses were obtained on a Hewlett-Packard 185B carbon hydrogen nitrogen analyzer. Electrospray ionization mass spectra were obtained on a Bruker micrOTOF spectrometer equipped with an electrospray ionization (ESI) source. The instrument was operated in both positive and negative ion mode using a 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 4.0 L/min. For ESI species were dissolved in MeOH or MeCN. In the isotopic pattern, the most intensive peak is reported. Infrared spectra (4000−400 cm^{-1}) were recorded on a Shimadzu FTIR 8400S instrument in KBr pellets. ^1H and $^{13}C\{^1H\}$ NMR spectra were measured on a Bruker-DPX 300 spectrometer at ambient temperature. TLC was carried out on Al plates precoated with a layer of Merck silica gel 60 F_{254}. For column chromatography Merck silica gel 60 F_{254} (0.063−0.200 mm) was used.

X-ray Crystal Structure Determinations. The crystals **5**, **7**, **8**·$CHCl_3$, and **9**·Me_2CO were immersed in cryo-oil, mounted in a nylon loop, and measured at a temperature of 100−120 K. The X-ray diffraction data were collected on a Nonius KappaCCD diffractometer using Mo Kα radiation (λ = 0.710 73 Å). The Denzo-Scalepack[72] or EvalCCD[73] program packages were used for cell refinements and data reductions. The structures were solved by direct methods using the SIR97[74] or SHELXS-97[75] program with the WinGX[76] graphical user interface. A semiempirical absorption correction (SADABS)[77] was applied to all data. Structural refinements were carried out using SHELXL-97.[75] The hydrogen atoms were positioned geometrically and constrained to ride on their parent atoms, with C−H = 0.95−0.98 Å and U_{iso} = 1.2−1.5U_{eq}-(parent atom). The crystallographic details are summarized in Table 1, and selected bond lengths and angles in Table 2. CCDC-789588−789591 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Synthetic Work. Cycloaddition of 1 (generated *in situ*) to the Ligated Nitriles. 3-Hydroxylamineisoborneol hydrochloride (**1**) (0.40 g, 1.8 mmol) was added to $RC(OEt)_3$ (R = Me, Et) (2.0 mmol) in CH_2Cl_2 (3 mL) and stirred at 40 °C for 2 h with A4 molecular sieves, whereupon Et_3N (0.18 g, 1.8 mmol) was added and the reaction mixture was stirred at 40 °C for additional 30 min. The progress of the reaction was monitored by TLC. Any of *trans*-$[PtCl_2(R'CN)_2]$ (R′ = Et, Ph, NMe_2) (0.5 mmol) was added to the prepared solution of **2** or **3**, and the reaction mixture was then stirred overnight at room temperature to give a pale yellow solution. The solvent was evaporated at room temperature to dryness, and the pale yellow, oily residue formed

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Table 1. Crystal Data

	5	**7**	**8**·$CHCl_3$	**9**·Me_2CO
empirical formula	$C_{38}H_{48}Cl_2N_4O_4Pt$	$C_{32}H_{52}Cl_2N_4O_4Pt$	$C_{41}H_{53}Cl_5N_4O_4Pt$	$C_{35}H_{60}Cl_2N_6O_5Pt$
fw	890.79	822.77	1038.21	910.88
temp (K)	100(2)	120(2)	100(2)	100(2)
λ (Å)	0.71073	0.71069	0.71073	0.71073
cryst syst	orthorhombic	orthorhombic	monoclinic	orthorhombic
space group	$P2_12_12_1$	$P2_12_12_1$	$P2_1$	$P2_12_12_1$
a (Å)	8.27490(10)	7.39480(10)	11.8983(2)	10.9605(2)
b (Å)	14.70990(10)	16.1571(3)	11.60150(10)	11.9222(2)
c (Å)	31.2056(2)	29.4684(6)	15.6181(2)	29.9856(6)
β (deg)	90	90	96.614(6)	90
V (Å^3)	3798.44(6)	3520.84(11)	2141.55(5)	3918.32(12)
Z	4	4	2	4
ρ_{calc} (Mg/m^3)	1.558	1.552	1.610	1.544
μ(Mo Kα) (mm^{-1})	3.879	4.177	3.633	3.764
no. reflns	81 469	30 341	44 066	70 273
unique reflns	11 101	8055	9279	11 436
GOOF (F^2)	1.057	1.019	0.962	1.025
R_{int}	0.0859	0.0402	0.0339	0.0548
R1[a] ($I \geq 2\sigma$)	0.0279	0.0287	0.0177	0.0277
wR2[b] ($I \geq 2\sigma$)	0.0495	0.0453	0.0347	0.0431

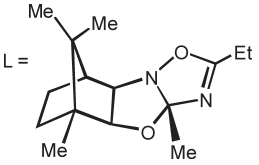
[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR2 = [\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]]^{1/2}$.

Table 2. Selected Bond Lengths (Å) and Angles (deg)

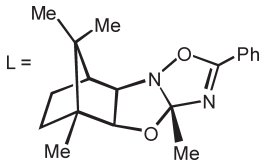
	5	**7**	**8**·$CHCl_3$	**9**·Me_2CO
Pt(1)−N(1)	2.015(3)	2.011(3)	2.006(2)	2.023(2)
Pt(1)−N(3)	2.021(2)	2.010(3)	2.002(2)	2.026(2)
Pt(1)−Cl(1)	2.3101(8)	2.3021(9)	2.2956(6)	2.3028(6)
Pt(1)−Cl(2)	2.2986(8)	2.2945(9)	2.3121(6)	2.3070(7)
N(1)−Pt(1)−N(3)	176.74(11)	177.38(12)	175.98(8)	178.43(9)
Cl(1)−Pt(1)−Cl(2)	176.19(3)	179.52(4)	179.55(2)	178.11(3)

was dissolved in CH_2Cl_2 (1 mL) and purified by column chromatography on SiO_2 (eluent: $CHCl_3$).

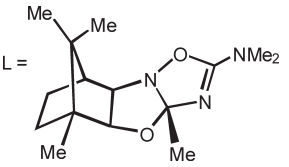
Characterization of *trans*-[$PtCl_2L_2$] (4−9). 4. Yield: 26.2 mg (66%). Anal. Found: C, 45.25; H, 6.09; N, 7.09. Calcd for $C_{30}H_{48}N_4Cl_2PtO_4$: C, 45.34; H, 6.09; N, 7.05. R_f = 0.59 (eluent $CHCl_3$/Me_2CO, 16:1, v/v). IR ν_{max} (KBr)/cm^{-1}: 2957 m (C−H), 1657 s (C═N). ^{1}H NMR δ_H (300 MHz, $CDCl_3$): 0.85 (3H, s, CH_3), 0.98 (3H, s, CH_3), 1.05 (3H, s, CH_3), 0.87−1.00 (2H, m, CH_2), 1.45 (4H, t + m, J = 7 Hz, CH_3 from Et and CH_2), 1.75 (1H, m, CH_2), 1.85 (3H, s, Me), 2.15 (1H, d, J 4 Hz, CH), 3.00 (1H, d, J = 7 Hz, CH), 3.03, 3.07 (2H, two m, J = 7 Hz, CH_2 from Et), 4.52 (1H, d, br, J = 7 Hz, CH). ^{13}C NMR δ_C (75.5 MHz, $CDCl_3$): 9.8 (CH_3), 11.1 (CH_3), 19.7 (CH_3), 22.5 (CH_3), 22.7 (CH_3), 24.2(CH_2), 25.8 (CH_2), 31.9 (CH_2), 46.8 (C^9), 48.1 (C^5), 48.7 (CH), 78.5 (CH), 88.5 (CH), 120.4 (C^{3a}), 172.8 (C_2). MS: m/z (high-resolution ESI$^+$) 795.386 (M + H, requires 795.273).



5. Yield 39.2 mg (88%). Anal. Found: C, 51.36; H, 5.53; N, 6.45. Calcd for $C_{38}H_{48}N_4Cl_2PtO_4$: C, 51.24; H, 5.43; N, 6.29. R_f = 0.65 ($CHCl_3$/Me_2CO, 16:1, v/v). IR ν_{max} (KBr)/cm^{-1}: 2957 m (CH), 1635 s (C═N). ^{1}H NMR δ_H (300 MHz, $CDCl_3$): 0.88 (3H, s, CH_3), 1.06 (3H, s, CH_3), 1.09 (3H, s, CH_3), 0.8−1.00 (2H, m, CH_2), 1.30−1.40 (1H, m, CH_2), 1.61−1.72 (1H, m, CH_2), 2.06 (3H, s, CH_3), 2.23 (1H, d, J = 4 Hz, CH), 3.19 (1H, d, J = 8 Hz, CH), 4.67 (1H, d, J = 8 Hz, CH), 7.65 (3H, m, Ph), 9.42 (2H, d, J = 7 Hz, Ph). ^{13}C NMR δ_C (75.5 MHz, $CDCl_3$): 11.1 (CH_3), 19.8 (CH_3), 22.6 (CH_3), 24.3 (CH_3), 25.6 (CH_2), 31.9 (CH_2), 47.0 (C^9), 48.0 (C^5), 48.6 (CH), 78.5 (CH), 88.8 (CH), 121.74 (C^{3a}), 123.4 (C_{ipso}), 128.9, 131.5, and 134.3 (Ph), 165.7 (C^2). MS: m/z (high-resolution ESI$^+$) 891.350 (M + H, requires 891.273). Crystals of **5** suitable for X-ray study were grown from $CHCl_3$ solution by a slow evaporation of the solvent at room temperature.

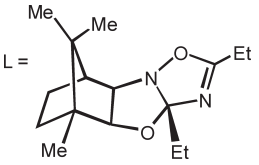


6. Yield: 37.1 mg (90%). Anal. Found: C, 43.73; H, 6.35; N, 9.82. Calcd for $C_{30}H_{50}N_6Cl_2PtO_4$: C, 43.69; H, 6.11; N, 10.19. R_f = 0.47 ($CHCl_3$/Me_2CO, 16:1, v/v). IR ν_{max} (KBr)/cm^{-1}: 2956 m-s (CH), 1669 s (C═N). ^{1}H NMR δ_H (300 MHz, $CDCl_3$): 0.82 (3H, s, CH_3), 0.88 (2H, m, CH_2), 0.98 (3H, s, CH_3), 0.99 (3H, s, CH_3), 1.42 (1H, m), 1.71 (1H, m)(CH_2), 1.83 (3H, s, CH_3), 2.08 (1H, d, J = 4 Hz, CH), 3.07 (1H, d, J = 8 Hz, CH), 3.60 (6H, s, br, NMe_2), 4.86 (1H, d, J = 8 Hz, CH). ^{13}C NMR δ_C (75.5 MHz, $CDCl_3$): 10.6 (CH_3), 19.3 (CH_3), 22.1 (CH_3), 24.8 (CH_3), 25.3 (CH_2), 31.7 (CH_2), 39.7 (br, NMe_2), 46.7 (C^9), 47.3 (CH), 47.9 (C^5), 76.6 (CH), 87.6 (CH), 118.3 (C^{3a}), 158.8 (C^2). MS: m/z (high-resolution ESI$^+$) 825.359 (M + H, requires 825.294).

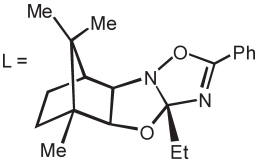


7. Yield: 29.6 mg (72%). Anal. Found: C, 46.85; H, 6.46; N, 6.81. Calcd for $C_{32}H_{52}N_4Cl_2PtO_4$: C, 46.71; H, 6.37; N, 6.81. R_f = 0.64 ($CHCl_3$/Me_2CO, 16:1, v/v). IR ν_{max} (KBr)/cm^{-1}: 2956 m (CH), 1658 s (C═N). ^{1}H NMR δ_H (300 MHz, $CDCl_3$): 0.83 (3H, s, CH_3), 0.96 (3H, s, CH_3), 1.04 (3H, s, CH_3), 0.86−1.00 (3H, m), 1.21−1.31 (3H, m), 1.35−1.51 (4H, m), 1.70−1.86 (2H, m, CH_2), 2.16 (1H, d, J = 4 Hz, CH), 3.03 (1H, d, J = 7 Hz, CH), 3.12−3.26 (2H, m, CH_2), 4.50−4.64 (1H, d, br, CH). ^{13}C NMR δ_C (75.5 MHz, $CDCl_3$): 8.4 (CH_3), 10.2 (CH_3), 11.1 (CH_3), 19.7 (CH_3), 22.5 (CH_3), 25.8 (CH_2), 29.8 (CH_2), 31.9 (CH_2), 22.6 (CH_2), 46.6 (C^9), 48.2 (C^5), 48.6 (CH), 78.5 (CH), 88.1 (CH), 122.4 (C^{3a}), 172.7 (C_2). MS: m/z (high-resolution ESI$^+$) 823.563 (M + H, requires 823.304),

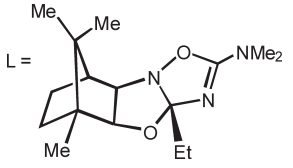
840.594 ([M + NH_4, requires 840.331). Crystals of **7** suitable for X-ray study were grown from a CH_2Cl_2 solution by a slow evaporation of the solvent at room temperature.



8. Yield: 32.6 mg (71%). Anal. Found: C, 49.54; H, 5.49; N, 5.35. Calcd for $C_{40}H_{52}N_4Cl_2PtO_4 \cdot 1/2CHCl_3$: C, 49.71; H, 5.41; N, 5.73. R_f = 0.70 ($CHCl_3/Me_2CO$, 16:1, v/v). IR ν_{max} (KBr)/cm^{-1}: 2957 m-s (CH), 1632 s (C═N). ^{1}H NMR δ_H (300 MHz, $CDCl_3$): 0.84 (3H, s, CH_3), 0.95 (3H, t, J = 7 Hz, CH_3), 1.03 (3H, s, CH_3), 1.08 (3H, s, CH_3), 0.8−1.00 (2H, m, CH_2), 1.30−1.40 (1H, m, CH_2), 1.63−1.80 (1H, m, CH_2), 1.96 (1H, m, J = 7 Hz, CH_2 from Et), 2.23 (1H, d, J = 4 Hz, CH), 3.08 (1H, q, J = 7 Hz, CH_2 from Et), 3.18 (1H, d, J = 8 Hz, CH), 4.66 (1H, d, J = 8 Hz, CH), 7.64 (3H, m, Ph), 9.39 (2H, d, J = 7 Hz, Ph). ^{13}C NMR δ_C (75.5 MHz, $CDCl_3$): 8.0 (CH_3), 10.8 (CH_3), 19.4 (CH_3), 22.1 (CH_3), 25.2 (CH_2), 29.4 (CH_2), 31.5 (CH_2), 46.3 (CH), 47.7 (C^9),48.1 (C^5), 77.8 (CH), 87.9 (CH), 122.8 (C^{3a}), 123.3 (C_{ipso}), 128.5, 131.1, and 133.8 (Ph), 165.6 (C^2). MS: m/z (high-resolution ESI$^+$) 919.429 (M + H, requires 919.304). Crystals of **8**·$CHCl_3$ suitable for an X-ray study were grown from a $CHCl_3$ solution by a slow evaporation of the solvent at room temperature.

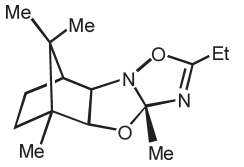


9. Yield: 33.3 mg (78%). Anal. Found: C, 44.80; H, 6.30; N, 9.61. Calcd for $C_{32}H_{54}N_6Cl_2PtO_4$: C, 45.07; H, 6.38; N, 9.85. R_f = 0.50 ($CHCl_3/Me_2CO$, 16:1, v/v). IR ν_{max} (KBr)/cm^{-1}: 2955 m-s (CH), 1669 s (C═N). ^{1}H NMR δ_H (300 MHz, $CDCl_3$): 0.84 (3H, s, CH_3), 0.88 (3H, t, J = 7.2 Hz, CH_3), 0.99 (3H, s, CH_3), 1.01 (3H, s, CH_3), 1.15−1.27 (1H, m), 1.42 (1H, m, CH_2), 1.72−1.78 (2H, m, J = 7.1 Hz, CH_2), 2.13 (1H, d, J = 4 Hz, CH), 2.78 (2H, m, CH_2), 3.08 (1H, d, J = 7 Hz, CH), 3.75 (6H, s, br, NMe_2), 4.90 (1H, d, J = 8 Hz, CH). ^{13}C NMR δ_C (75.5 MHz, $CDCl_3$): 8.1 (CH_3), 10.7 (CH_3), 19.4 (CH_3), 22.1 (CH_3), 25.4 (CH_2), 30.4 (CH_2), 31.8 (CH_2), 39.8 (br, NMe_2), 46.5 (CH), 47.4 (C^9), 48.0(C^5), 77.6 (CH), 87.1 (CH), 120.5 (C^{3a}), 159.4 (C^2). MS: m/z (high-resolution ESI$^+$) 853.413 (M + H, requires 853.326). Crystals of **9**·Me_2CO suitable for an X-ray study were grown from an acetone solution by a slow evaporation of the solvent at room temperature.

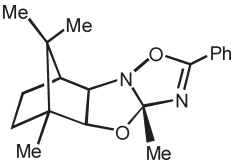


Liberation of Dihydro-1,2,4-oxadiazoles from 4, 5, 7, and 8. An excess of NaCN (11.8 mg, 0.24 mmol) in methanol-d_4 (0.5 mL) was added to a solution of the corresponding [$PtCl_2$(dihydro-1,2,4-oxadiazole)$_2$] complex **4**, **5**, **7**, and **8** (0.03 mmol) in CD_2Cl_2 (0.5 mL), and the reaction mixture was left to stand at 35 °C; completeness of the reaction was monitored by ^{1}H NMR. During this time, the initially pale yellow solution turned colorless, and the colorless precipitate of NaCl and the known $Na_2[Pt(CN)_4]$[78,79] (ESI$^-$-MS 149.4894, calcd 149.4885) was formed. Free heterocycles were separated from excess NaCN (and also from NaCl and $Na_2[Pt(CN)_4]$ formed in the reaction) by evaporation of the solvent at room temperature and treating the colorless, oily residue with CH_2Cl_2. The liquid phase was separated by filtration, and evaporation of the solvent afforded heterocycles **10**−**13** as colorless, oily residues in almost quantitative yields.

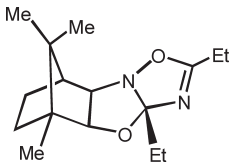
10. ^{1}H NMR δ_H (300 MHz, $CDCl_3$): 0.82 (3H, s, CH_3), 0.90 (2H, m, CH_2), 1.000 (6H, s, two CH_3), 1.22 (3H, t, J = 7.5 Hz, CH_3), 1.44 (1H, m, CH_2), 1.57 (3H, s, CH_3), 1.73 (1H, m, CH_2), 2.13 (1H, d, J 4 Hz, CH), 2.34 (1H, q, J = 7.5 Hz, CH_2), 3.02 (1H, d, J = 7 Hz, CH), 3.82 (1H, d, J = 7 Hz, CH). ^{13}C NMR δ_C (75.5 MHz, $CDCl_3$): 10.1 (CH_3), 10.8 (CH_3), 19.4 (CH_3), 20.3 (CH_2), 22.1 (CH_3), 23.8 (CH_3), 25.6 (CH_2), 31.7 (CH_2), 46.2 (C^9), 47.7 (C^5), 48.5 (CH), 78.3 (CH), 87.1 (CH), 121.5 (C^{3a}), 167.9 (C^2). MS: m/z (high-resolution ESI$^+$) 265.192 (M + H, requires 265.192).



11. ^{1}H NMR δ_H (300 MHz, $CDCl_3$): 0.86 (3H, s, CH_3), 0.87−1.00 (2H, m, CH_2), 1.03 (3H, s, CH_3), 1.07 (3H, s, CH_3), 1.20 (1H, m, CH_2), 1.70 (3H, s, CH_3), 1.71−1.78 (1H, m, CH_2), 2.22 (1H, d, J = 4 Hz, CH), 3.19 (1H, d, J = 8 Hz, CH), 3.90 (1H, d, J = 8 Hz, CH), 7.47 (2H, m, *m*-Ph), 7.55 (1H, m, *p*-Ph), 7.98 (2H, d, J = 7 Hz, *o*-Ph). ^{13}C NMR δ_C (75.5 MHz, $CDCl_3$): 10.7 (CH_3), 19.5 (CH_3), 22.2 (CH_3), 23.8 (CH_3), 25.6 (CH_2), 31.7 (CH_2), 46.3 (C^9), 47.8 (C^5), 48.5 (CH), 78.2 (CH), 87.3 (CH), 121.9 (C^{3a}), 125.5 (C_{ipso}), 128.6, and 132.3 (Ph), 162.7 (C^2). MS: m/z (high-resolution ESI$^+$) 313.192 (M + H, requires 313.192).



12. ^{1}H NMR δ_H (300 MHz, $CDCl_3$): 0.82 (3H, s, CH_3), 0.90−0.98 (5H, m + t, CH_2 and CH_3), 0.94 (3H, s, CH_3), 0.98 (6H, s, CH_3), 1.24 (3H, t, J = 7.5 Hz, CH_3), 1.43 (1H, m), 1.78 (2H, m, two CH_2), 1.98 (1H, m, CH_2), 2.14 (1H, d, J = 4.5 Hz, CH), 2.35 (2H, q, J = 7.5 Hz, CH_2), 3.03 (1H, d, J = 7.3 Hz, CH), 3.81 (1H, d, J = 7.5 Hz, CH). ^{13}C NMR δ_C (75.5 MHz, $CDCl_3$): 7.7 (CH_3), 10.3 (CH_3), 10.8 (CH_3), 19.4 (CH_3), 20.4 (CH_2), 22.1 (CH_3), 25.7 (CH_2), 30.7 (CH_2), 31.7 (CH_2), 46.0 (C^9), 47.8 (C^5), 48.4 (CH), 78.8 (CH), 86.7 (CH), 123.7 (C^{3a}), 167.9 (C^2). MS: m/z (high-resolution ESI$^+$) 279.211 (M + H, requires 279.207).



13. ^{1}H NMR δ_H (300 MHz, $CDCl_3$): 0.85 (3H, s, CH_3), 0.89 (3H, t, J = 7 Hz, CH_3), 1.02 (3H, s, CH_3), 1.05 (3H, s, CH_3),

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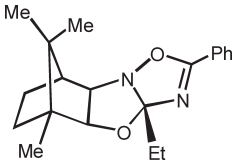
(79) Kharitonov, Y. Y.; Evstaf'eva, O. N.; Baranovskii, I. B.; Mazo, G. Y.; Babaeva, A. V. *Zh. Neorg. Khim.* **1966**, *11*, 1733.

0.85−1.00 (2H, m, CH_2), 1.15 (1H, m, CH_2), 1.74 (1H, m, CH_2), 1.93 (1H, m, J = 7 Hz, CH_2 from Et), 2.10 (1H, m, J = 7 Hz, CH_2 from Et), 2.22 (1H, d, J = 4 Hz, CH), 3.19 (1H, q, J = 7 Hz, CH_2 from Et), 3.18 (1H, d, J = 8 Hz, CH), 3.89 (1H, d, J = 8 Hz, CH), 7.48 (3H, m, Ph), 7.98 (2H, d, J = 7 Hz, Ph). ^{13}C NMR δ_C (75.5 MHz, $CDCl_3$): 7.7 (CH_3), 10.8 (CH_3), 19.5 (CH_3), 22.1 (CH_3), 25.6 (CH_2), 30.8 (CH_2), 31.7 (CH_2), 46.1 (C^9), 47.8 (C^5), 48.4 (CH), 78.7 (CH), 87.0 (CH), 124.0 (C^{3a}), 125.5 (C_{ipso}), 128.5, 130.8, and 132.2 (Ph), 162.6 (C^2). MS: m/z (high-resolution ESI$^+$) 327.207 (M + H, requires 327.207).



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Supporting Information Available: Synthesis of enantiomerically pure chiral nitrones, crystallographic data in CIF format, and crystal structures of **5**, **8**·$CHCl_3$, and **9**·Me_2CO (Figures S1−S3). This material is available free of charge via the Internet at http://pubs.acs.org.