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Pt^{II}-Mediated 1,3-Dipolar Cycloaddition of Oxazoline *N*-Oxides to Nitriles as a Key Step to Dihydrooxazolo-1,2,4-oxadiazoles

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A novel type of heterocycle, viz., 2,3a-disubstituted 5,6-dihydro-3a*H*-[1,3]oxazolo[3,2-*b*][1,2,4]oxadiazoles, was generated by an intermolecular Pt^{II}-mediated 1,3-dipolar cycloaddition (1,3-DCA) between the oxazoline *N*-oxide $C(Me)_2CH_2OC(R)=N^+(O^-)$ (R = Me, Et) and coordinated nitriles in the complexes *trans*/*cis*-$[PtCl_2(R'CN)_2]$ [R′ = Me, Et, CH_2Ph, Ph, $N(C_5H_{10})$]. The reaction is unknown for free RCN and oxazoline *N*-oxides, but under Pt^{II}-mediated conditions, it proceeds smoothly (CH_2Cl_2, 20–25 °C, 18–20 h) and gives pure complexes $[PtCl_2\{N=C(R')ONC(R)OCH_2CMe_2\}_2]$ [R/R′ = Me/Me, **1**; Me/Et, **2**; Me/CH_2Ph, **3**; Me/Ph, **4**; Me/$N(C_5H_{10})$, **5**; Et/Me, **6**; Et/Et, **7**; Et/CH_2Ph, **8**; Et/Ph, **9**; Et/$N(C_5H_{10})$, **10**] in 42–84% yields after column chromatography. Compounds **1**–**10** were characterized by elemental analyses (C, H, N), FAB^+-MS, IR, and ^1H and $^{13}C\{^1H\}$ NMR spectroscopies, and X-ray diffraction (for **1**, **2**, **5**, and **9**). With the exception of benzonitrile complexes, 1,3-DCA of oxazoline *N*-oxides to the Pt^{II}-ligated nitriles occurred diastereoselectively and afforded mixtures of enantiomers. Depending on the substituents on nitriles, asymmetric atoms in both of the formed heterocyclic ligands have the same (*SS*/*RR*) or different (*SR*/*RS*) configurations. The heterocyclic ligands were liberated from **1**–**4** and **6**–**9** by treatment with excess ethane-1,2-diamine (en) in CH_2Cl_2 for 1 day at 20–25 °C (for R′ = Me, Et, CH_2Ph) and at 50 °C (for R′ = Ph) to achieve the free organic species and the well-known $[Pt(en)_2](Cl)_2$; the products were separated, and 2,3a-disubstituted 5,6-dihydro-3a*H*-[1,3]oxazolo[3,2-*b*][1,2,4]oxadiazoles (**11**–**18**) were characterized by ESI^+-MS and ^1H and $^{13}C\{^1H\}$ NMR spectroscopies.

Introduction

In contrast to the wide utility of nitriles as synthons in organic synthesis, their use in cycloaddition (CA) chemistry is rather limited. Nitriles are involved in some Diels−Alder processes or react with dipoles in 1,3-dipolar cycloadditions (1,3-DCAs) but at elevated temperatures, unless reactions are intramolecular[1] or a nitrile bears a strong electron-withdrawing group.[1] The development of new methods for accelerating the CA to nitriles and the performance of these reactions under mild conditions is an important area of chemical research.

Among various methods for the activation of nitriles, their coordination to a metal center has become a widespread synthetic technique and it allows the performance of such reactions that are uncommon or even not feasible for the corresponding noncoordinated species.[2] In this context, the activation of nitriles *toward nucleophilic attack* received much attention[3,4] and various metal centers proved to be useful for this kind of transformation. However, the transition-metal-mediated activation of the C≡N bond *toward CA* has been paid incomparably less attention from the stand-

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points of synthetic coordination and organic chemistry, although the first reviews on the subject have been published.[5,6]

The latter, a rather uncommon mode of nitrile activation in 1,3-DCAs, was investigated mostly for azides by Purcell et al.,[7] Hay and McLaren,[8] and recently by Sharpless et al.[9] and also, by some of us, for metal-mediated reactions of RCN with nitrones[10−13] and nitrile oxides.[14] Our experimental[10,14] and theoretical[15,16] results demonstrate that the coordination of RCN to Pt centers dramatically enhances the reactivity of the nitriles toward dipoles of both allyl- and propargyl/allenyl anion types in comparison with CA to uncomplexed RCN species. In particular, nitriles coordinated to a Pt^{IV} center undergo CA with aromatic and aliphatic nitrones under very mild conditions.[10] The nitriles in the corresponding Pt^{II} complexes exhibit a slightly lower reactivity,[11] while at Pd^{II} centers the CA demonstrates lower selectivity[12] owing to the ability of Pd^{II} to coordinate O atoms of dipoles along with coordination of the dipolarophile RCN. All of these indicate that the Lewis acidity and hard/soft properties of the metal play important roles in the reaction control.[6]

Being interested in amplification of the Pt-mediated 1,3-DCA reactions to other dipoles, we launched a project aimed to verify, by theoretical methods, various factors affecting the CA and found that the coordination of RCN to a Pt center ought to provide even a higher activation effect upon CA in comparison with the introduction of such a powerful electron-acceptor group R as CF_3.[15,16] Furthermore, the calculations show that the reactivity of oxazoline *N*-oxides (IUPAC:[17] 4,5-dihydrooxazole-3-oxides **A**; Figure 1) toward metal-mediated 1,3-DCA to RCN is expected to be higher in comparison with the previously investigated acyclic nitrones (**B1** and **B2**). It is worthwhile mentioning that oxazoline *N*-oxides have efficiently been employed for 1,3-DCAs to diverse C═C double and C≡C triple bonds (including those functionalized with the nitrile group, which remains intact after the CA), giving a significant number of ring systems with useful properties.[18,19] In contrast, the reaction of oxazoline *N*-oxides with the nitrile C≡N moiety has never been observed in the past. This is probably because of, on the one hand, the low reactivity of the nitrile group toward dipoles[2,6] and, on the other hand, the substantial instability of the known oxazoline *N*-oxides.[19−21]

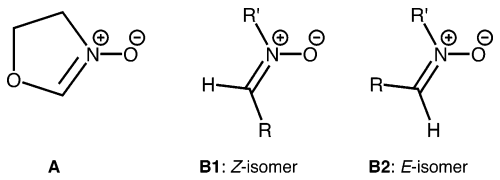

Figure 1.

Bearing in mind the theoretical results outlined in the previous paragraph, we were not surprised to find that ligated nitriles attached to a Pt^{II} center are highly competent partners for CA reactions with oxazoline *N*-oxides, and all of these results are described in the Article. To our knowledge, this report covers the first example of the direct synthesis of a novel type heterocycle, viz., IUPAC:[17] 2,3a-disubstituted 5,6-dihydro-3a*H*-[1,3]oxazolo[3,2-*b*][1,2,4]oxadiazoles; generated by an intermolecular Pt^{II}-mediated 1,3-DCA between an oxazoline *N*-oxide and coordinated nitrile.

Experimental Section

Instrumentation and Materials. C, H, and N elemental analyses were carried out by the Department of Organic Chemistry of the St.Petersburg State University. Positive-ion electrospray ionization time-of-flight (ESI-TOF) mass spectra of **11**−**18** were obtained on a MX-5310 mass spectrometer, using 1:1 (v/v) H_2O/CH_3CN as the solvent stream; the probe concentration was ca. 10^{-5} M. Spectra were recorded in a *m*/*z* range comprised between 10 and 3000 Da: flow rate 10 μL/min, spray tip potential 3.3 kV, nozzle potential 50.00 V, skimmer voltage 18.00 V, nozzle temperature 40 °C. Positive-ion fast atom bombardment (FAB) mass spectra of the Pt^{II}

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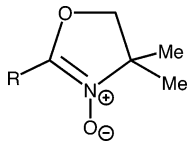

Figure 2. Oxazoline *N*-oxides employed for the 1,3-DCAs: R = Me (**C**); Et (**D**).

complexes were obtained on a MS-50C (Kratos) instrument by bombarding 3-nitrobenzyl alcohol matrices of the samples with 8 keV (ca. 1.28×10^{15} J) Xe atoms. Thin-layer chromatography (TLC) was performed on Merck on 60 F_{254} SiO_2 plates. IR 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 in $CDCl_3$ on a Bruker AMX-300 spectrometer at ambient temperature.

Solvents were obtained from commercial sources and used as received. In the series $[PtCl_2(R'CN)_2]$ [R′ = Me, Et, CH_2Ph, Ph, $N(CH_2)_5$], the former complex was obtained as a mixture of the *cis*- and *trans*-$[PtCl_2(MeCN)_2]$ isomers in a ratio of ca. 5:1 by the known method,[22] while the other compounds were prepared as pure trans isomers in accordance with the published procedures.[23] Oxazoline *N*-oxides (**C** and **D**; Figure 2) were synthesized from $RC(OEt)_3$ (R = Me and Et, respectively) and 2-(hydroxylamino)-2-methyl-1-propanol by the literature method.[20,21]

X-ray Crystal Structure Determinations. The crystals of **1**, **2**, **5**, and **9** were obtained by slow evaporation of the solvent from a $CHCl_3$ or $CDCl_3$ solution of the corresponding complexes. The crystals were immersed in cryo-oil, mounted in a nylon loop, and measured at a temperature of 105−150 K. The X-ray diffraction data were collected by means of a Nonius Kappa CCD diffractometer using Mo Kα radiation (λ = 0.710 73 Å). The *Denzo-Scalepack*[24] or *EvalCCD*[25] program packages were used for cell refinements and data reductions. The structures were solved by direct methods using *SHELXS-97*,[26] *SIR-97*,[27a] or *SIR-2004*[27b] with the *WinGX*[28] graphical user interface. An empirical absorption correction was applied to all of the data (*XPREP* in *SHELXTL*, version 6.14-1,[29] or *SADABS*, version 2.10[30]). Structural refinements were carried out using *SHELXL-97*.[31] The D atom of $CDCl_3$ in **9** was refined isotropically. Other H atoms were positioned geometrically and were also constrained to ride on their parent atoms with C−H = 0.95−0.99 Å and $U_{iso} = 1.2-1.5U_{iso}$ (parent atom). The crystallographic details for **1**, **2**, **5**, and **9** are summarized in Table 1 and the selected bond lengths and angles in Table 2.

Pt^{II}-Mediated 1,3-DCA (a General Procedure). (i) In Situ Synthesis of Oxazoline *N*-Oxides. A suspension of 2-(hydroxylamino)-2-methyl-1-propanol (50 mg, 0.36 mmol) in dichloromethane (1 mL) was added to triethyl orthoacetate (70 mg, 0.45 mmol) for **C** or triethyl orthopropionate (80 mg, 0.45 mmol) for **D**, and the reaction mixture was stirred at room temperature for 1 h, whereupon triethylamine (0.05 mL, 0.36 mmol) was added and the solution was stirred at room temperature for 15 min.

(ii) CA Reactions. This solution was added to a suspension of *trans*-$[PtCl_2(R'CN)_2]$ [0.12 mmol; R′ = Me, Et, CH_2Ph, Ph; $N(C_5H_{10})$] in CH_2Cl_2 (2 mL). The reaction mixture was stirred at room temperature for 24 h to give a pale-yellow solution, whereupon the solvent was evaporated at room temperature. The pale-yellow oily residue formed was dissolved in CH_2Cl_2 (1 mL) and purified by column chromatography (see later). Evaporation of the solvent gave the pale-yellow crystalline residue. Yield: 65−70%. Below we provide characterizations of the complexes $[PtCl_2L_2]$, where L is depicted in Figure 3.

***cis/trans*-1 (cis/trans Isomers in a Ratio of 2:1 Based on ^1H NMR Integration).** Anal. Calcd for $C_{16}H_{28}N_4Cl_2O_4Pt$: C, 31.69; H, 4.65; N, 9.24. Found: C, 31.29; H, 4.51; N, 8.92. TLC: R_f = 0.37 [eluent: 1:10 (v/v) $Me_2CO/CHCl_3$]. FAB^+-MS: *m/z* 629 [M + Na]$^+$. IR spectrum (KBr, selected bands, cm^{-1}): 1658 ν(C═N). ^1H NMR [δ (ppm), *J* (Hz)]: 1.09 (trans), 1.25 (cis), 1.27 (trans), and 1.32 (cis) (four s, 6H, CH_3C^6), 2.04 (trans) and 2.21 (cis) (two s, 3H, CH_3C^2), 2.67 (cis) and 2.69 (trans) (two s, 3H, CH_3C^{3a}), 3.12 and 3.67 (cis, two d, *J* = 8.4), 3.51 and 3.74 (trans, two d, *J* = 9.3, 2H, C$^5H_2$). In the cis/trans isomeric mixture, attribution of signals is based on the spectra of the individual trans isomer obtained in the reaction between *trans*-**1** and nitrone **C**. For *trans*-**1.** ^1H NMR [δ (ppm), *J* (Hz)]: 1.09, 1.27, (two s, 6H, CH_3C^6), 2.04 (s, 3H, CH_3C^2), 2.69 (s, 3H, CH_3C^{3a}), 3.51 and 3.74 (two d, *J* = 9.3, 2H, C$^5H_2$). ^{13}C NMR [δ (ppm)]: 13.6 (*C*H$_3$C^2), 18.6, 19.7, 23.2, 24.8, and 27.7 (*C*H$_3$C^6 and *C*H$_3$C^{3a}), 68.3 (C^6), 72.3 and 72.9 (C^5); the resonances from C^2 and C^{3a} were not observed. Yield: 46% (33.5 mg).

2. Anal. Calcd for $C_{18}H_{32}N_4Cl_2O_4Pt$: C, 34.07; H, 5.08; N, 8.83. Found: C, 34.26; H, 5.08, N, 8.85. TLC: R_f = 0.58 [eluent: 1:10 (v/v) $Me_2CO/CHCl_3$]. FAB^+-MS: *m/z* 562 [M − 2HCl]$^+$, 633 [M − H]$^+$, 657 [M + Na]$^+$. IR spectrum (KBr, selected bands, cm^{-1}): 1657 ν(C═N). ^1H NMR [δ (ppm), *J* (Hz)]: 1.26 and 1.28 (two s, 6H, CH_3C^6), 1.44 (t, *J* = 7.3, 3H, CH_3CH$_2$C^2), 2.05 (s, 3H, CH_3C^{3a}), 3.08−3.15 and 3.28−3.33 (two m, 2H, CH_2C^2), 3.30 and 3.74 (two d, *J* = 9.2, 2H, C$^5H_2$). ^{13}C NMR [δ (ppm)]: 10.1 (*C*H$_3$CH$_2$C^2), 20.0, 22.2, and 26.3 (*C*H$_3$C^6, CH$_3$C^{3a}, and CH$_2$C^2), 69.2 (C^6), 73.2 (C^5), 119.9 (C^{3a}), 176.5 (C^2). Yield: 70% (53.3 mg).

3. Anal. Calcd for $C_{28}H_{36}N_4Cl_2O_4Pt$: C, 44.33; H, 4.78; N, 7.39. Found: C, 44.43; H, 4.91; N, 7.22. TLC: R_f = 0.58 [eluent: 1:10 (v/v) $Me_2CO/CHCl_3$]. FAB^+-MS: *m/z* 711 [M − 2Cl + Na]$^+$, 735 [M − 2Cl + 2Na]$^+$. IR spectrum (KBr, selected bands, cm^{-1}): 1644 ν(C═N). ^1H NMR [δ (ppm), *J* (Hz)]: 0.95 and 1.19 (two s, 6H, CH_3C^6), 2.11 (s, 3H, CH_3C^{3a}), 3.43 and 3.69 (two d, *J* = 9.2, 2H, C$^5H_2$), 4.26 and 4.85 (two d, *J* = 15.3, 2H, CH_2C^2), 7.36 and 7.48 (two m, 5H, PhCH_2C^2). ^{13}C NMR [δ (ppm)]: 19.6, 25.6, and 26.3 (*C*H$_3$C^{3a} and CH$_3$C^6), 34.4 (*C*H$_2$PhC^2), 62.4 (C^6), 72.7 (C^5), 116.7 (C^{3a}), 127.8, 128.6, 129.2, and 132.3 (*C*−Ph), 170.9 (C^2). Yield: 84% (76.5 mg).

4. Anal. Calcd for $C_{26}H_{32}N_4Cl_2O_4Pt$: C, 42.75; H, 4.42; N, 7.67. Found: C, 42.58; H, 4.48; N, 7.58. TLC: R_f = 0.63 [eluent: 1:10

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Table 1. Crystallographic Data for **1**, **2**, **5**, and **9**

	1	**2**	**5**	**9**·2CDCl$_3$
empirical formula	$C_{16}H_{28}Cl_2N_4O_4Pt$	$C_{18}H_{32}Cl_2N_4O_4Pt$	$C_{28}H_{36}Cl_2N_4O_4Pt$	$C_{26}H_{42}D_2Cl_8N_6O_4Pt$
fw	606.41	634.47	758.60	985.37
temp (K)	120(2)	150(2)	105(2)	120(2)
λ (Å)	0.710 73	0.710 73	0.710 73	0.710 73
cryst syst	monoclinic	monoclnic	monoclinic	triclinic
space group	*C*2/*c*	*C*2/*c*	$P2_1/n$	$P\bar{1}$
a (Å)	20.1567(5)	20.5932(6)	9.4537(7)	9.1351(9)
b (Å)	9.6656(2)	9.1472(4)	10.5337(5)	9.9820(4)
c (Å)	12.1219(2)	14.4093(4)	15.6088(11)	10.0486(6)
α (deg)	90	90	90	81.645(5)
β (deg)	116.455(2)	117.766(3)	105.088(6)	88.340(6)
γ (deg)	90	90	90	86.454(6)
V (Å^3)	2114.36(9)	2401.75(16)	1500.78(17)	904.65(11)
Z	4	4	2	1
ρ_{calc} (Mg/m^3)	1.905	1.755	1.679	1.809
λ(Mo Ka) (mm^{-1})	6.918	6.094	4.892	4.510
no. of reflns	11 503	10 359	8440	18 943
no. of unique reflns	2421	2354	2948	4132
R_{int}	0.0521	0.0692	0.0343	0.0210
R1[a] ($I \geq 2\sigma$)	0.0188	0.0415	0.0217	0.0131
wR2[b] ($I \geq 2\ \sigma$)	0.0456	0.0949	0.0381	0.0301

[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) for **1**, **2**, **5**, and **9**

	1	**2**	**5**	**9**
Pt1−N1	2.036(2)	2.012(5)	2.0164(12)	2.011(2)
Pt1−Cl1	2.2951(6)	2.305(2)	2.3057(4)	2.2930(9)
N1−C6	1.472(3)	1.483(8)	1.4632(19)	1.478(4)
N1−C1	1.278(3)	1.272(9)	1.299(2)	1.277(4)
O1−N2	1.480(3)	1.475(8)	1.4622(16)	1.468(4)
N2−C2	1.509(4)	1.502(9)	1.508(2)	1.503(4)
C6−O2	1.419(3)	1.409(8)	1.4065(19)	1.395(4)
Cl1−Pt1−N1	87.94(6)	88.60(16)	89.58(4)	87.61(7)
N1−C6−O2	110.4(2)	111.8(5)	106.64(12)	111.3(3)
O1−N2−C2	107.1(2)	108.4(5)	109.13(11)	109.3(3)

(v/v) $Me_2CO/CHCl_3$]. FAB$^+$-MS: *m/z* 634 [M − H]$^+$. IR spectrum (KBr, selected bands, cm^{-1}): 1656 ν(C═N). ^{1}H NMR [δ (ppm), *J* (Hz)]: (a mixture of diastereomers in a ratio of 1:1): 1.33, 1.34, 1.36, and 1.39 (four s, 6H, CH_3C^6), 2.10, 2.15, 2.19, and 2.30 (four s, 3H, CH_3C^{3a}), 3.71−3.78 (m, 2H, CH_2C^5), 7.43 (t, *J* = 7.7, *p*-Ph), 7.60 (m, *o*- and *m*-Ph), 8.69 (t, *J* = 7.7, *p*-Ph), 9.18 (two d, *J* = 7.2, *o*-Ph, 5H, *H*−Ph). ^{13}C NMR [δ (ppm)]: 19.8, 26.0, 26.1, 26.2, 27.2, and 27.9 (*C*H$_3$C^{3a} and *C*H$_3$C^6), 69.0 (C^6), 73.1, 73.2, and 73.3 (C^5), 120.7, 121.0, and 121.1 (C^{3a}), 122.3, 128.3, 128.6, 130.2, 130.5, 130.6, 133.1, and 133.6 (*C*−Ph), 167.2 (C^2). Yield: 75% (65.7 mg).

5. Anal. Calcd for $C_{24}H_{42}N_6Cl_2O_4Pt{\cdot}H_2O$: C, 37.80; H, 5.81; N, 11.02. Found: C, 38.85; H, 5.78; N, 10.95. TLC: R_f = 0.64 [eluent: 1:10 (v/v) $Me_2CO/CHCl_3$]. FAB$^+$-MS: *m/z* 671 [M − Cl]$^+$, 744 [M]$^+$. IR spectrum (KBr, selected bands, cm^{-1}): 1651 ν(C═N). ^{1}H NMR [δ (ppm), *J* (Hz)]: 1.22 and 1.24 (two s, 6H, CH_3C^6), 1.58−1.93 (m, 6H, CH_2), 1.99 (s, 3H, CH_3C^{3a}), 3.61 and 4.00 (two d and d, *J* = 8.7, 2H, H_2C^5), 4.15−4.70 (m, 4H, NCH_2). ^{13}C NMR [δ (ppm)]: 20.3, 24.3, and 25.9 (*C*H$_3$C^{3a}, *Me*C^6), 27.4, 28.4, and 48.8 (*C*H$_2$), 67.6 (C^6), 73.6 (C^5), 119.8 (C^{3a}), 157.7 (C^2). Yield: 61% (54.5 mg).

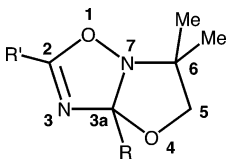


Figure 3. 2,3a-Disubstituted 5,6-dihydro-3a*H*-[1,3]oxazolo[3,2-*b*][1,2,4]-oxadiazoles (L) with an atom numbering scheme.

***cis/trans*-6 (cis/trans Isomers in a Ratio of 1:2 Based on ^{1}H NMR Integration).** Anal. Calcd for $C_{18}H_{32}N_4Cl_2O_4Pt$: C, 34.07; H, 5.08; N, 8.83. Found: C, 34.10; H, 5.19; N, 8.67. TLC: R_f = 0.49 [eluent: 1:5 (v/v) $Me_2CO/CHCl_3$]. FAB$^+$-MS: *m/z* 658 [M − 2HCl]$^+$, 695 [M − HCl]$^+$. IR spectrum (KBr, selected bands, cm^{-1}): 1658 ν(C═N). ^{1}H NMR [δ (ppm), *J* (Hz)]: 1.11 (trans) and 1.12 (cis) (two t, *J* = 8.0, 3H, CH_3CH$_2$C^{3a}), 1.24, 1.26, 1.29, and 1.32 (four s, 6H, CH_3C^6), 2.00, 2.20, 2.54, and 2.78 (four m, 2H, CH_2C^{3a}), 2.54 (cis) and 2.69 (trans) (two s, 3H, CH_3C^2), 3.08 and 3.63 (two d, *J* = 8.7, cis), 3.51 and 3.74 (two d, *J* = 9.2, trans, 2H, H_2C^5). ^{13}C NMR [δ (ppm)]: 8.8 and 9.2 (*C*H$_3$CH$_2$C^{3a}), 14.3, 14.5, 20.3, 20.9, 25.3, and 25.8 (*C*H$_3$C^2 and *C*H$_3$C^6), 32.7 and 33.2 (*C*H$_2$C^{3a}), 68.1 and 68.5 (C^6), 73.0 and 73.8 (C^5), 122.3 and 122.8 (C^{3a}), 170.0 and 170.5 (C^2). Yield: 70% (53.3 mg). In the cis/trans isomeric mixture, attribution of signals is based on the spectra of the pure trans isomer obtained in the reaction between *trans*-$[PtCl_2(EtCN)_2]$ and nitrone **D**. Trans isomer. ^{1}H NMR [δ (ppm), *J* (Hz)]: 1.17 (t, *J* 8.0, 3H, CH_3CH$_2$C^{3a}), 1.24 and 1.25 (two s, 6H, CH_3C^6), 2.21 and 2.49 (four m, 2H, CH_2C^{3a}), 2.72 (s, 3H, CH_3C^2), 3.70 (m, 2H, H_2C^5). ^{13}C NMR [δ (ppm)]: 8.8 (*C*H$_3$CH$_2$C^{3a}), 14.2, 20.2, 20.9, and 26.8 (*C*H$_3$C^2 and *C*H$_3$C^6), 31.6 (*C*H$_2$C^{3a}), 68.5 (C^6), 73.8 (C^5), 122.5 (C^{3a}); C^2 was not detected.

7. Anal. Calcd for $C_{20}H_{36}N_4Cl_2O_4Pt$: C, 36.26; H, 5.48; N, 8.46. Found: C, 35.06; H, 5.09; N, 8.55. TLC: R_f = 0.67 [eluent: 1:10 (v/v) $Me_2CO/CHCl_3$]. FAB$^+$-MS: *m/z* 629 [M − Cl]$^+$. IR spectrum (KBr, selected bands, cm^{-1}): 1658 ν(C═N). ^{1}H NMR [δ (ppm), *J* (Hz)]: 1.15 (t, *J* = 7.9, 3H, CH_3CH$_2$C^{3a}), 1.23 and 1.25 (two s, 6H, CH_3C^6), 1.47 (t, *J* = 9.2, 3H, CH_3CH$_2$C^2), 2.20 and 2.52 (two m, 2H, CH_2C^{3a}), 3.15 and 3.31 (two m, 2H, CH_2C^2), 3.50 and 3.71 (two d, *J* = 8.7, 2H, H_2C^5). ^{13}C NMR [δ (ppm)]: 8.3 and 9.7 (*C*H$_3$-CH$_2$C^2 and *C*H$_3$CH$_2$C^{3a}), 19.6 and 23.5 (*Me*C^6), 26.3 and 31.1 (*C*H$_2$C^{3a}, *C*H$_2$C^2), 67.9 (C^6), 73.2 (C^5), 121.9 (C^3), 161.3 (C^2). Yield: 66% (52.5 mg).

8. Anal. Calcd for $C_{30}H_{40}N_4Cl_2O_4Pt$: C, 45.80; H, 5.13; N, 7.12. Found: C, 45.87; H, 5.17; N, 7.02. TLC: R_f = 0.67 [eluent: 1:10 (v/v) $Me_2CO/CHCl_3$]. FAB$^+$-MS: *m/z* 784 [M − H]$^+$, 808 [M + Na]$^+$. IR spectrum (KBr, selected bands, cm^{-1}): 1651 ν(C═N). ^{1}H NMR [δ (ppm), *J* (Hz)]: 0.93 and 1.18 (two s, 6H, CH_3C^6), 1.16 (t, *J* = 7.8, 3H, CH_3CH$_2$C^{3a}), 2.29 and 2.59 (two m, br, 2H,

CH_2C^{3a}), 3.63 and 3.68 (two d, J = 9.2, 2H, C$^5H_2$), 4.33 and 4.89 (two d, J = 15.3, 2H, CH_2C^2), 7.32 and 7.57 (two m, 5H, H−Ph). ^{13}C NMR [δ (ppm)]: 8.4 (*C*H$_3$CH$_2$C^{3a}), 19.2 and 26.4 (*C*H$_3$C^6), 31.3 and 34.7 (*C*H$_2$C^{3a}, *C*H$_2$C^2), 68.2 (C^6), 73.5 (C^5), 122.3 (C^{3a}), 127.8, 128.8, 129.5, and 132.0 (*C*−Ph), 168.7 (C^2). Yield: 79% (74.6 mg).

9. Anal. Calcd for $C_{28}H_{36}N_4Cl_2O_4Pt$: C, 44.33; H, 4.78; N, 7.39. Found: C, 44.10; H, 4.80; N, 7.29. TLC: R_f = 0.59 and 0.64 [eluent: 1:10 (v/v) $Me_2CO/CHCl_3$]. FAB$^+$-MS: *m/z* 686 [M − 2HCl]$^+$, 759 [M]$^+$. IR spectrum (KBr, selected bands, cm^{-1}): 1631 ν(C═N). ^{1}H NMR [δ (ppm), J (Hz)]: (a mixture of diastereomers in a 1:1 ratio) 1.02 (t, J = 8.0) and 1.15 (t, J = 8.1) (3H, C*H*$_3$-CH$_2$C^{3a}), 1.31, 1.33, 1.36, and 1.38 (four s, 3H, C*H*$_3$C^6), 2.13, 2.30, 2.62, and 2.77 (four m, 2H, C*H*$_2$C^{3a}), 3.68−4.08 (two d and m, J = 9.5 and 8.7, 2H, H_2C^5), 7.44 (m, *p*-Ph), 7.60 (m, *o*- and *m*-Ph), 8.69 (m, *p*-Ph), 9.25 (m, *o*-Ph, 5H, H−Ph). ^{13}C NMR [δ (ppm)]: 8.6 (*C*H$_3$CH$_2$C^{3a}), 20.0, 26.8, and 27.0 (*C*H$_3$C^6), 31.1, 31.2, and 31.7 (*C*H$_2$C^{3a}), 67.7 and 68.0 (C^6), 74.1 and 74.2 (C^5), 122.5 and 122.8 (C^{3a}), 123.7, 123.8, and 124.0 (C$_{ipso}$), 128.4, 128.6, 128.7, 130.3, 130.5, 130.7, 130.9, 133.1, and 133.8 (*C*−Ph), 166.0 (C^2). Yield: 77% (70.1 mg).

10. Anal. Calcd for $C_{26}H_{46}N_6Cl_2O_4Pt$: C, 40.42; H, 6.00; N, 10.88. Found: C, 40.20; H, 5.90; N, 10.79. TLC: R_f = 0.63 [eluent: 1:5 (v/v) $Me_2CO/CHCl_3$]. FAB$^+$-MS: *m/z* 773 [M]$^+$. IR spectrum (KBr, selected bands, cm^{-1}): 1655 ν(C═N). ^{1}H NMR [δ (ppm), J (Hz)]: 0.96 and 0.98 (two t, J = 6.54, 3H, C*H*$_3$CH$_2$C^{3a}), 1.22 and 1.26 (two s, 6H, C*H*$_3$C^6), 1.69 and 1.85 (two m, br, 6H, C*H*$_2$), 1.99 and 2.59 (two m, 2H, C*H*$_2$C^{3a}), 3.68 and 4.25 (d and two d, J = 8.7, 2H, H_2C^5), 4.30−4.70 (m, 4H, NC*H*$_2$). ^{13}C NMR [δ (ppm)]: 9.2 (*C*H$_3$CH$_2$C^{3a}), 20.4, 24.4, and 25.9 (*C*H$_3$C^{3a}, *Me*C^6), 28.1, 32.1, and 48.9 (*C*H$_2$), 67.6 (C^6), 74.2 (C^5), 122.1 (C^{3a}), 158.5 (C^2). Yield: 42% (38.9 mg).

Liberation of 3a-R′-2-R-5,6-dihydro-3a*H*-[1,3]oxazolo[3,2-*b*]-[1,2,4]oxadiazoles from Complexes 1−4 and 6−9. An excess of neat ethane-1,2-diamine (en; 60 mg, 2.0 mmol) was added to a solution of the corresponding [PtCl$_2$L$_2$] complex (0.05 mmol) in dichloromethane (2 mL), and the reaction mixture was stirred for 1 day at 20−25 °C (R′ = Me, Et, CH_2Ph) and 1 day at 50 °C in MeCN (R′ = Ph). In the cases of R′ = Me, Et, and CH_2Ph, during this time, the initially pale-yellow solution turned practically colorless and the colorless precipitate of the known[32] [Pt(en)$_2$](Cl)$_2$ complex was formed. The addition of water (0.5 mL) to the reaction mixture results in dissolution of the solid and gives a pale-yellow aqueous phase along with a colorless organic layer; the latter was separated, washed with water, and dried with Na_2SO_4. In the case of R′ = Ph, the solvent was evaporated at room temperature and an oily residue formed was partially dissolved upon the addition of CH_2Cl_2 followed by the addition water to give two layers. The dichloromethane layer was separated and dried with Na_2SO_4. In all cases, evaporation of the solvent afforded heterocycles **11**−**18** as colorless oily residues in almost quantitative yields. The heterocycles from complexes **5** and **10** were not liberated even for 1 week at 35 °C.

11. ESI$^+$-MS: *m/z* 171 [M + H]$^+$. ^{1}H NMR [δ (ppm), J (Hz)]: 1.29 and 1.34 (two s, 6H, C*H*$_3$C^6), 2.22 (s, 3H, C*H*$_3$C^2), 2.68 (s, 3H, C*H*$_3$C^{3a}), 3.13 and 3.69 (two d, J = 8.3, 2H, H_2C^5). ^{13}C NMR [δ (ppm)]: 11.5 (*C*H$_3$C^2), 20.3 and 25.5 (*C*H$_3$C^6), 26.6 (*C*H$_3$C^{3a}), 67.2 (C^6), 72.0 (C^5), 121.3 (C^{3a}), 163.6 (C^2). Yield: 55% (9.4 mg).

12. ESI$^+$-MS: *m/z* 207 [M + Na]$^+$. ^{1}H NMR [δ (ppm), J (Hz)]: 1.26 (t, J = 7.7, 3H, C*H*$_3$CH$_2$C^2), 1.28 and 1.29 (two s, 6H, C*H*$_3$C^6), 1.77 (s, 3H, C*H*$_3$C^{3a}), 2.34 (q, J = 7.7, 2H, C*H*$_2$C^2), 3.22 and 3.67 (two d, J = 8.7, 2H, C^5). ^{13}C NMR [δ (ppm)]: 10.9 (*C*H$_3$CH$_2$C^2), 19.3 (*C*H$_2$C^2), 20.1, 25.4, and 26.5 (*C*H$_3$C^{3a}, *C*H$_3$C^6), 69.2 (C^6), 73.2 (C^5), 121.2 (C^{3a}), 168.3 (C^2). Yield: 73% (13.4 mg).

13. ESI$^+$-MS: *m/z* 247 [M + H]$^+$. ^{1}H NMR [δ (ppm), J (Hz)]: 1.09 and 1.20 (two s, 6H, C*H*$_3$C^6), 1.77 (s, 3H, C*H*$_2$C^{3a}), 3.03 and 3.59 (two d, J = 8.4, 2H, H_2C^5), 3.61 and 3.71 (two d, J = 14.8, 2H, C*H*$_2$C^2), 7.32 (m, 5H, CH$_2$*Ph*). ^{13}C NMR [δ (ppm)]: 20.0 and 25.6 (*Me*C^6), 26.8 (*C*H$_2$C^{3a}), 32.8 (*C*H$_2$C^2), 67.4 (C^6), 72.2 (C^5), 1241.4 (C^{3a}), 127.3, 128.7, and 128.8 (*C*−Ph), 134.2 (C$_{ipso}$), 165.4 (C^2). Yield: 86% (22.4 mg).

14. ESI$^+$-MS: *m/z* 233 [M + H]$^+$. ^{1}H NMR [δ (ppm), J (Hz)]: 1.34, 1.39 (two s, 6H, C*H*$_3$C^6), 1.89 (s, 3H, C*H*$_3$C^{3a}), 3.31 and 3.74 (two d, J = 9.3, 2H, H_2C^5), 7.46 (m, 2H, *m*-Ph), 7.56 (m, 1H, *p*-Ph), 7.95 (d, J = 7.2, 2H, *o*-Ph). ^{13}C NMR [δ (ppm)]: 20.4 and 25.7 (*Me*C^6), 26.8 (*C*H$_3$C^2), 67.6 (C^6), 72.3 (C^5), 124.6 (C^{3a}), 128.5 (*o*- and *m*-Ph), 132.3 (*p*-Ph), 162.4 (C^2). Yield: 15% (3.5 mg).

15. ESI$^+$-MS: *m/z* 185 [M + H]$^+$. ^{1}H NMR [δ (ppm), J (Hz)]: 1.01 (t, 3H, J = 7.3, C*H*$_3$CH$_2$C^{3a}), 1.22 and 1.27 (two s, 6H, C*H*$_3$C^6), 1.85 and 2.07 (two m, 2H, C*H*$_2$C^{3a}), 2.05 (s, 3H, C*H*$_3$C^2), 3.23 and 3.66 (two d, J = 8.9, 2H, H_2C^5). ^{13}C NMR [δ (ppm)]: 8.4 (*C*H$_3$CH$_2$C^{3a}), 11.5 (*C*H$_3$C^2), 20.4 and 25.7 (*C*H$_3$C^6), 32.3 (*C*H$_2$C^{3a}), 66.9 (C^6), 71.9 (C^5), 124.0 (C^{3a}), 163.7 (C^2). Yield: 80% (14.6 mg).

16. ESI$^+$-MS: *m/z* 221 [M + Na]$^+$. ^{1}H NMR [δ (ppm), J (Hz)]: 1.02 (t, 3H, J = 7.7, C*H*$_3$CH$_2$C^{3a}), 1.23, 1.25, and 1.28 (t and two s, 9H, C*H*$_3$CH$_2$C^2 and C*H*$_3$C^6), 1.86 and 2.12 (two m, 2H, C*H*$_2$C^{3a}), 2.38 (q, J = 7.7, 2H, C*H*$_2$C^2), 3.23 and 3.66 (two d, J = 8.7, 2H, H_2C^5). ^{13}C NMR [δ (ppm)]: 8.9 (*C*H$_3$CH$_2$C^{3a}), 11.7 (*C*H$_3$CH$_2$C^2), 19.9 (*C*H$_2$C^2), 20.7 and 26.2 (*Me*C^6), 32.7 (*C*H$_2$C^{3a}), 67.3 (C^6), 72.2 (C^5), 124.4 (C^{3a}), 168.4 (C^2). Yield: 84% (16.7 mg).

17. ESI$^+$-MS: *m/z* 261 [M + H]$^+$. ^{1}H NMR [δ (ppm), J (Hz)]: 1.01 (t, 3H, J = 7.8, C*H*$_3$CH$_2$C^{3a}), 1.08 and 1.18 (two s, 6H, C*H*$_3$C^6), 1.87 and 2.11 (two m, 2H, C*H*$_2$C^{3a}), 3.06 and 3.59 (two d, J = 8.8, 2H, H_2C^5), 3.64 and 3.73 (two d, J = 14.8, 2H, C*H*$_2$C^2), 7.33 (m, 5H, CH$_2$*Ph*). ^{13}C NMR [δ (ppm)]: 8.5 (*C*H$_3$CH$_2$C^{3a}), 20.0 and 25.8 (*Me*C^6), 32.7 (*C*H$_2$C^{3a}), 32.9 (*C*H$_2$C^2), 67.1 (C^6), 72.0 (C^5), 124.1 (C^{3a}), 127.3, 128.7, and 128.8 (*C*−Ph), 134.3 (C$_{ipso}$), 165.5 (C^2). Yield: 85% (22.1 mg).

18. ESI$^+$-MS: *m/z* 247 [M + H]$^+$. ^{1}H NMR [δ (ppm), J (Hz)]: 1.08 (t, 3H, J = 7.4, C*H*$_3$CH$_2$C^{3a}), 1.31, 1.38 (two s, 6H, and C*H*$_3$C^6), 1.98 and 2.23 (two m, 2H, C*H*$_2$C^{3a}), 3.30 and 3.73 (two d, J = 9.2, 2H, H_2C^5), 7.46 (m, 2H, *m*-Ph), 7.55 (m, 1H, *p*-Ph), 7.96 (d, J = 7.4, 2H, *o*-Ph). ^{13}C NMR [δ (ppm)]: 8.5 (*C*H$_3$CH$_2$C^{3a}), 20.4 and 25.9 (*Me*C^6), and 32.5 (*C*H$_2$C^{3a}), 67.3 (C^6), 72.1 (C^5), 124.6 (C^{3a}), 128.5 (*o*- and *m*-Ph), 132.2 (*p*-Ph), 162.5 (C^2). Yield: 33% (8.1 mg).

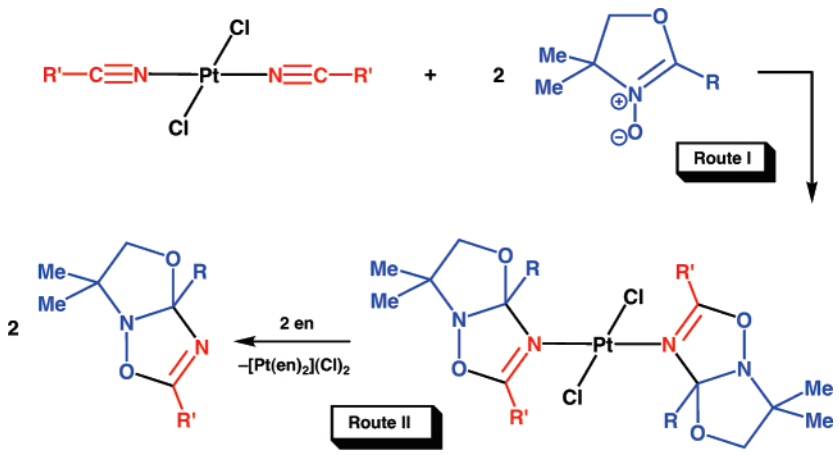
Results and Discussion

We have previously demonstrated that Pt^{IV} centers activate nitrile substrates toward 1,3-DCA of nitrile oxides in a significantly more effective way than Pt^{II} centers; the latter have almost no effect on this reaction.[33] In the current work, we found that the activation of RCN by Pt^{IV} centers toward 1,3-DCA is so significant that the reaction loses its selectivity and the formation of a broad of mixture of products was observed. Unlikely, a Pt^{II} center provides a sufficient activation to perform the reaction and to make it selective.

Metal-Mediated 1,3-DCA of Oxazoline *N*-Oxides to (Nitrile)platinum(II) Complexes. The oxazoline *N*-oxides **C** and **D** were obtained in situ by a known method,[20,21] which includes the reaction between $HOCH_2C(Me)_2NHOH\cdot HCl$

(32) Jörgensen, S. M. *J. Prakt. Chem.* **1889**, *39*, 1.

Scheme 1



R/R′	Me	Et	CH_2Ph	Ph
Me	**11**	**12**	**13**	**14**
Et	**15**	**16**	**17**	**18**

R/R′	Me	Et	CH_2Ph	Ph	$N(C_5H_{10})$
Me	**1**	**2**	**3**	**4**	**5**
Et	**6**	**7**	**8**	**9**	**10**

and $RC(OEt)_3$ (R = Me, Et) in CH_2Cl_2 followed by the addition of NEt_3. The solution of **C** (or **D**) prepared by this method was added to a solution [R′ = Et, CH_2Ph, Ph, $N(C_5H_{10})$] or suspension (R′ = Me) of *trans*/*cis*-$[PtCl_2(R'CN)_2]$ in CH_2Cl_2; a molar ratio of the reactants was ca. 3:1. After 18−20 h, the reaction mixture was evaporated in a flow of N_2 to ca. one-fourth of the initial volume and then the target material was purified by column chromatography on SiO_2. Characterization of the products (see later) revealed that the reactions of *trans*/*cis*-$[PtCl_2(R'CN)_2]$ with oxazoline *N*-oxides **C** and **D** afforded the dihydrooxazolo-1,2,4-oxadiazole complexes Pt^{II} (Scheme 1, route I).

Complexes **1**−**10** were isolated as yellow solids and characterized by elemental analyses (C, H, N), FAB^+-MS, IR, and ^1H and $^{13}C\{^1H\}$ NMR spectroscopies, and X-ray data (for **1**, **2**, **5**, and **9**). Thus, the complexes gave satisfactory microanalysis and the expected fragmentation/isotopic pattern in FAB^+-MS; the typical ions that were detected are $[M]^+$, $[M + Na]^+$, and $[M - HCl]^+$. A comparison of the IR spectra of **1**−**10** with those of the starting materials shows the absence of the ν(C≡N) stretching vibrations at ca. 2300 cm^{-1}, and the availability of strong ν(C═N) vibrations emerged in the range between 1630 and 1660 cm^{-1}.

For all complexes, signal integration in the ^1H NMR spectra gives evidence that the reaction between each of the coordinated nitrile and an oxazoline *N*-oxide proceeds in a 1:1 ratio. ^1H NMR spectra of **1**−**10** display the characteristic doublets of the C^5 protons in the range between 3.08 and 4.25 ppm. In the $^{13}C\{^1H\}$ NMR spectra of these complexes, peaks due to C^2═N (157.7−176.5 ppm) and C^{3a} (116.7−122.8 ppm) were recognized. Both ^1H and $^{13}C\{^1H\}$ NMR spectra of compounds **1** and **6** exhibit two sets of signals in ratios of 2:1 and 1:2, respectively, derived from the cis and trans isomers. Characteristic doublets of the C^5 protons for the trans complexes are low-field-shifted from those for the appropriate cis forms.

NMR data also show that the CA occurred diastereoselectively for compounds **1**−**3**, **5**−**8**, and **10**. Thus, the ^1H NMR spectra of *trans*-**1**−**3** and **6**−**8** display one set of signals due to an enantiomeric mixture with the same (*SS*/*RR*) configuration of both C^{3a} and C'^{3a} atoms, while for **5** and **10**, one of the two HC^5 protons gives two signals of very close chemical shift values (the difference is less than 0.01 ppm). These two resonances belong to two bicyclic moieties of different (*R* and *S*) configuration. In the $^{13}C\{^1H\}$ NMR spectra, peaks from the asymmetric C^{3a} carbons are also duplicate, and this fact gives an additional argument that favors the formation of another pair of enantiomers. The ^1H and $^{13}C\{^1H\}$ NMR spectra of **4** and **9** show several sets of signals probably due to the formation of a diastereomeric (*RR*/*SS*/*RS*) mixture (see later for a discussion of the stereochemistry of the CA).

The CA described in this section is Pt^{II}-mediated. Indeed, it was proved in a separate experiment that the most electron-deficient nitrile of the series, i.e., PhCN, in $CDCl_3$ in the absence of the metal center does not react with the dipoles at 50 °C for 20 h and only gradual degradation of the oxazoline *N*-oxides was observed under those conditions. Moreover, the coordination increases the polarization of the C≡N bond, and this make the CA highly regioselective.[15,16]

X-ray Structure Determinations of (Dihydrooxazolo-1,2,4-oxadiazole)platinum(II) Complexes. In **1**, the bicyclic ligands lie in the cis position to each other, while compounds **2**, **5**, and **9** exhibit the trans configuration. The Pt1−N1 bond lengths in the complexes are typical for (imine)platinum(II) species; the Pt1−N1 bond length in **1** [2.036(2) Å] is slightly longer than those [2.011(2)−2.0164(12) Å] in **2**, **5**, and **9** probably because of a higher ground-state trans influence of the Cl ligand compared to the imine N. In **1**, **2**, **5**, and **9**, the bond distances N1−C1 [1.272(9)−1.299(2) Å] in the bicyclic ligands are typical for the N═C double bond,[34] while the N1−C6 bond lengths [1.4632(19)−1.483(8) Å] belong

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(34) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans.* **1987**, *2*, S1.

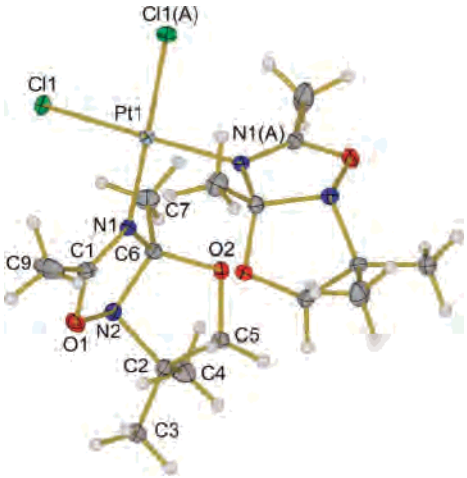

Figure 4. Thermal ellipsoid view of complex **1** with an atomic numbering scheme. The only *RR* enantiomer from the *RR*/*SS* pair is shown, and thermal ellipsoids are drawn at 50% probability.

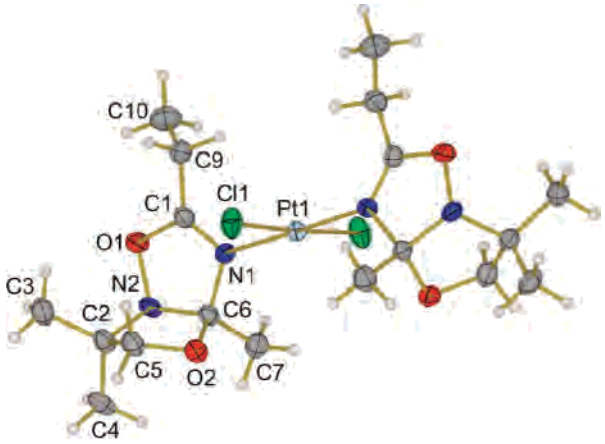

Figure 5. Thermal ellipsoid view of complex **2** with an atomic numbering scheme. The only *RR* enantiomer from the *RR*/*SS* pair is shown, and thermal ellipsoids are drawn at 50% probability.

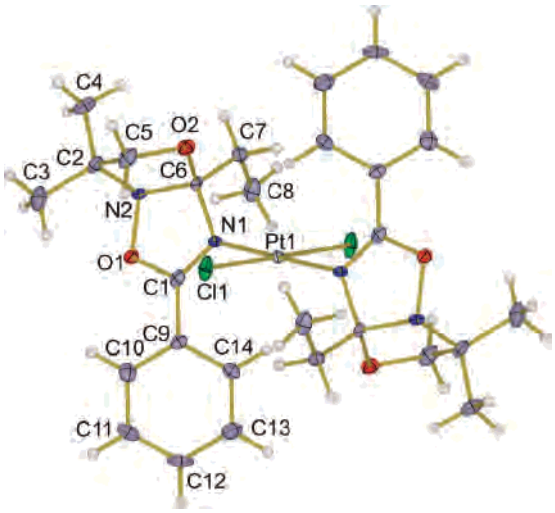

Figure 6. Thermal ellipsoid view of complex **5** (a mixture of *RS*/*SR* enantiomers) with an atomic numbering scheme. Thermal ellipsoids are drawn at 50% probability. The $CDCl_3$ solvent has been omitted for clarity.

to the typical N−C single bonds. In **1** and **2**, both asymmetric atoms C^{3a} in the heterocyclic ligands have the same configuration (*RR* and *SS* in the enantiomeric mixture of the complexes), while in **5** and **9**, two ligands exhibit different configurations (*RS*). In **1**, the {N1C1O1N2C6} planes of two cyclic ligands are oriented with a 74.65(8)° angle to each other to minimize steric repulsion. In **2**, the torsion angle between such planes is less [i.e., 24.8(3)°], and in centrosymmetric **5** and **9**, the {N1C1O1N2C6} planes are coplanar.

Stereochemistry of the 1,3-DCA. CA to the nitrile ligands in the starting complexes, in principle, could give the heterocyclic ligands having *RR*, *SS*, and *RS* configurations of the C^{3a} and C'^{3a} atoms. We observed that the stereoselectivity of these reactions is different depending on the R′ group in the complexed nitrile dipolarophiles. Thus, 1,3-DCA of nitrones **C** and **D** to the nitrile ligands in cis/trans mixtures of the $[PtCl_2(MeCN)_2]$ complex proceeds diastereoselectively and leads to cis/trans mixtures of **1** or **6**, respectively. The NMR spectra of the products display two sets of peaks corresponding to enantiomeric mixtures of the cis and trans complexes (see above and also the Experimental Section). It was also detected that during the reactions a ratio between cis and trans isomers has been changed from 5:1 in the starting complex $[PtCl_2(MeCN)_2]$ to 2:1 in **1** and 1:2 in **6**, correspondingly. These mixtures were not separated by chromatography because of the very close retention indexes of the isomers, and ratios between isomers were verified by ^1H NMR integration.

In CA, the change in the proportion between the cis and trans isomers in solution occurs as a result of the thermal cis-to-trans isomerization; the latter proceeds in accordance with the isomerization principle[1b,35] for square-planar complexes. Complex *cis*-**1** has been structurally characterized (Figure 4), and the X-ray data show that in the mixture of enantiomeric complexes both C^{3a}-asymmetric atoms in the heterocycles formed and, consequently, the dihydrooxazolo-1,2,4-oxadiazoles have the same configuration (*RR* and *SS*).

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1,3-DCA of nitrones **C** and **D** to EtCN in *trans*-$[PtCl_2(EtCN)_2]$ also occurs diastereoselectively and in the cases of **2** and **7** brings about the formation of enantiomers showing a sole set of signals in the NMR spectra. The X-ray diffraction data for complex **2** (Figure 5) indicate that the C^{3a} atoms of both dihydrooxazolo-1,2,4-oxadiazole ligands, similarly to **1**, have the same configuration. The NMR spectra of **3** and **7** (the latter obtained in the reaction between **C** and **D** and pure *trans*-$[PtCl_2(PhCH_2CN)_2]$) also favor the diastereoselectivity of the CA. It is worthwhile mentioning that in the case of the Pt^{II} complex with the push-pull nitrile, i.e., *trans*-$[PtCl_2\{(CH_2)_5NCN\}_2]$, another pair of enantiomers is formed in 1,3-DCA. The X-ray data for **5** (Figure 7) show that the C^{3a} atoms of the heterocyclic ligands have the *RS* configuration. In **5** and **10**, a different configuration (*R* and *S*) of two bicyclic moieties is supported by NMR data (see above).

In the case of the benzonitrile complexes, CA does not occur diastereoselectively and the NMR spectra display a few sets of resonances due to a mixture of diastereomers (*RR*/*SS*/*RS*). An X-ray study for **9** (Figure 6) verified different

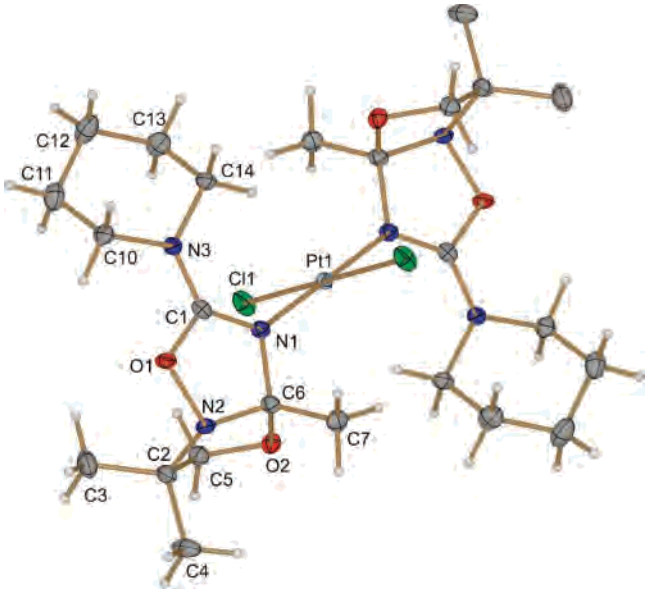

Figure 7. Thermal ellipsoid view of complex **9** (a mixture of *RS*/*SR* enantiomers) with an atomic numbering scheme. Thermal ellipsoids are drawn at 50% probability. The solvent molecule $CDCl_3$ has been omitted for clarity.

enantiomers (*R* and *S*) of the dihydrooxazolo-1,2,4-oxadiazole ligands. The absence of stereoselectivity for $[PtCl_2(PhCN)_2]$ is probably due to intra/intermolecular interactions of the phenyl ring, or it can be rationalized by the least steric hindrance of Ph[36] among other R′ groups of the series.

Ligand Liberation and Characterization of the Free Heterocycles. In the past few years, several methods for liberation of imines from their Pt^{II} complexes have been developed, and they are based on displacement with an excess of diphosphines[37] or thiourea.[38] We observed that the newly formed heterocyclic ligands in **1**−**10** are so strongly bound to the Pt^{II} center that liberation cannot be achieved even with 1,2-bis-(diphenylphosphino)ethane. However, we succeeded in releasing the ligands for all complexes besides two (i.e., **5** and **10**), and the free $C^{3a}{}_{R/S}$ enantiomeric dihydrooxazolo-1,2,4-oxadiazoles were liberated by treatment with excess en in CH_2Cl_2 for 1 day at 20−25 °C (for R′ = Me, Et, CH_2Ph) and at 50 °C (for R′ = Ph) (Scheme 1, route II). In the latter case, the heterocyclic ligands are strongly bound in complexes **4** and **9**, and their liberation should be performed at the higher temperature. Under these conditions, the free dihydrooxazolo-1,2,4-oxadiazoles are not stable, and therefore they were isolated only in moderate yields (15% for **14** and 33% for **18**). In the other cases, the ligands were obtained in 55−86% yields. In complexes **5** and **10**, the dihydrooxazolo-1,2,4-oxadiazoles derived from 1,3-DCA to the so-called push-pull nitrile $(C_5H_{10})NC{\equiv}N$ are strongly bound to the Pt^{II} center. They were liberated only under prolonged heating (5 days at 50 °C) of their MeCN solutions with en or with $NH_2CH_2CH_2NHCH_2CH_2NH_2$. However, under these conditions the heterocycles are not stable, and they were decomposed right after liberation to give a mixture of yet unidentified products.

In the liberation reactions, the known[32] complex $[Pt(en)_2](Cl)_2$ is formed as the other product along with the free ligand. The hydrophilic complex $[Pt(en)_2](Cl)_2$ and the excess of en were separated from the hydrophobic heterocycle upon washing of the residue (R = Ph) or the reaction mixture (R = Me, Et, CH_2Ph) with water.

After the separation, the dihydrooxazolo-1,2,4-oxadiazoles were subject to ^1H and $^{13}C\{^1H\}$ NMR monitoring in $CDCl_3$ and the same sample was additionally analyzed by ESI-MS. These data are given in the Experimental Section, and they unequivocally confirm the decoordination of the heterocycles and support their formulation. Thus, ESI^+-MS spectra display peaks that can be attributed to $[M + H]^+$ or $[M + Na]^+$. ^1H and $^{13}C\{^1H\}$ NMR spectra contain one set of signals; in ^1H NMR, C^5 protons emerge as two doublets in the ranges of 3.22−3.64 and 3.66−3.73 ppm. In **11**−**18**, $^{13}C\{^1H\}$ NMR spectra show peaks from $C^2{=}N$ (162.5−168.4 ppm) and C^{3a} (121.2−124.6 ppm) atoms.

Final Remarks

The reaction described in this Article is the first example of the CA between oxazoline *N*-oxides and nitriles, and it can be applied to the direct synthesis performed under mild conditions and using easily prepared Pt^{II} compounds of the previously inaccessible families of 2,3a-disubstituted 5,6-dihydro-3a*H*-[1,3]oxazolo[3,2-*b*][1,2,4]oxadiazoles and their metal complexes. The reaction has a general character, and it was successfully employed to various activated (with acceptor groups, e.g., Ph) and nonactivated (with donor groups, e.g., Me) nitriles RCN and even to the so-called push-pull species [R = $N(CH_2)_5$].

The presence of the Pt^{II} center at the nitrile group was found to be essential for the reactivity. Indeed, even the rather electron-deficient nitrile PhCN in the uncomplexed form does not react with the oxazoline *N*-oxides, while endeavors to conduct this reaction under more drastic conditions failed because of the well-known[18,20,21] thermal instability of oxazoline *N*-oxides, resulting in their degradation in advance of the attempted CA.

In accordance with our previous theoretical calculations, the role of the Pt^{II} center in the normal electron-demand CA reaction[15,16] comes to *selective* coordination of the dipolarophile RCN to a Pt center, and this complexation significantly lowers the $HOMO_{dipole}-LUMO_{dipolarophile}$ gap between the reactants, thus facilitating the interplay. Hence, involvement of a soft and kinetically inert Pt metal center, which reacts selectively with the dipolarophile and does not affect the dipole, is crucial for these CAs. The skeptical reader, however, may feel some dissatisfaction with the use of the Pt starting material, which makes the suggested synthesis

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of 2,3a-disubstituted 5,6-dihydro-3a*H*-[1,3]oxazolo[3,2-*b*]-[1,2,4]oxadiazoles rather expensive. We still believe that the Pt^{II}-mediated CA is so far the only route to these types of heterocycles, and for a while, we should be satisfied just with achieving these compounds by any means. In addition, the conventional recycling[39] of Pt might strongly reduce all expenses associated with this two-step synthetic transformation.

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Supporting Information Available: Crystallographic data in CIF format. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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