Orthoplatination of Primary Amines

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The first efficient and general cycloplatination reaction of primary amines is introduced. A precursor obtained from K_2PtCl_4 and HI undergoes fast substitution by amine ligands; the resulting *trans* diamine derivative is converted via C−H activation into a cycloplatinated square-planar complex. The reaction proceeds surprisingly fast, under mild conditions and with high yields, even for electron-deficient substrates. The monohapto amine ligand in the product complex may be substituted by alternative donor ligands such as phosphanes or pyridine derivatives. Single-crystal X-ray diffraction studies of a *trans* compound which is suggested as intermediate, of three target complexes involving electronically different primary amines and of four substitution products are reported and underline the broad range of products accessible by this synthesis.

Introduction

ortho-Metalation of amines with palladium and platinum share a common history: As early as 1968, Cope and Friedrich reported C−H activation for electron-rich amines and imines.[1] The two noble metals differ, however, significantly in cyclometalation. In general, the reaction proceeds with much higher yields and for a wider range of substrates in the case of palladium;[2] the initial restriction rules for cyclopalladation no longer apply.[3] On the other hand, "cycloplatination", the formation of a C−Pt bond in a metallacycle, even today remains a challenge. From a kinetic point of view, Pt(II) represents one of the most inert metal centers in coordination chemistry, and therefore most reactions proceed much slower than for the lighter congener palladium. No general precursor for cycloplatination has been found to date: The reaction of *N,N*-dimethylbenzylamine with the standard platinum source K_2PtCl_4 gives at best a yield of 20%.[1] With the same reagent, secondary or primary amines fail to *ortho*-metalate. In 1997, *cis*-$PtCl_2(dmso)_2$ emerged as a more promising reagent,[4] but even with this starting material successful examples of *ortho*-platination are limited to tertiary amines. For ferrocenylamines, the same precursor proved to undergo facile cycloplatination. Despite the good performance of these reactions with tertiary ferrocenylamines, no experimental procedure has yet been reported for cyclometalation of primary or secondary ferrocenylamines.[5] We are not aware of any well-documented and convenient general method for the synthesis of primary *ortho*-platinated amines at the preparative scale. A recent communication[6] explicitly gives a yield of 10% for a benzylamine derivative and underlines the difficulties in systematically synthesizing this class of compounds; the authors state, "It is interesting to point out that, in spite of initial difficulties well established methods have now been developed for the cyclopalladation of primary amines, however, the preparation of platinum analogues still remains uncommon."

In view of the experimental difficulties with the synthesis of cycloplatinated primary amines, the almost entire lack of structural information for these compounds is no surprise: Only one crystal structure of a benzylamine derivative[7] is documented in the Cambridge Structural Database.[8] Basic research interests apart, motivation for the synthesis and structural elucidation of cycloplatinated primary amines also stems from recent interest in organoplatinum compounds as potential antitumor drugs.[9,10]

Results and Discussion

In the context of our quest for a straightforward and general synthesis from primary amines to the cycloplatinated target molecules we have identified the reaction product of potassium tetrachloroplatinate with hydroiodic acid as a suitable precursor. In contrast to our initial idea, the resulting dark powder cannot simply be addressed as pure K_2PtI_4, which was structurally characterized by Olsson and Oskarsson.[11] X-ray diffraction rather shows the additional presence of at least one more crystalline phase: Several lines in the powder pattern match those calculated for K_2PtI_5.[12] The chemical reactivity of the precursor also suggests a more complex nature than K_2PtI_4: We recall that Pt(II) compounds are notoriously inert; the presence of one or more platinum complexes in a higher oxidation state can explain the short reaction times and mild conditions required for cycloplatination. Although the quantitative composition of the precursor varies with subtle details in its preparation, it does not affect the subsequent cycloplatination step relevant for this work. We note that Corain and Poë observed the formation of

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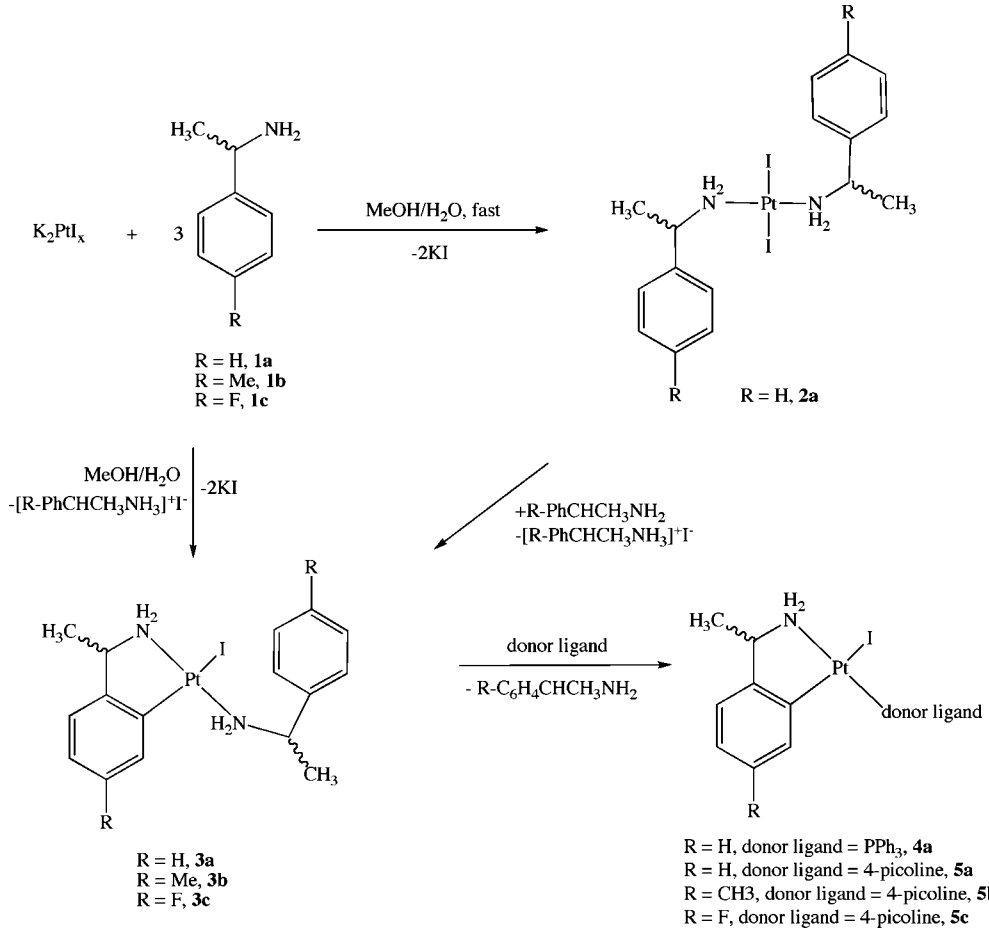
Scheme 1. Synopsis of the Reaction Pathways and Products



Pt complexes with a "higher oxidation state than II" under similar preparation conditions as early as 1967.[13]

The potassium iodoplatinate precursor and the primary amine form the intermediate complex *trans*-PtI_2L_2, **2**, which in a second step undergoes *ortho*-platination to **3**. Scheme 1 compiles the reaction sequence and the compounds prepared by this method.

The *ortho*-platination may also be conducted as a "one-pot reaction", starting from K_2PtCl_4; in this case, the iodoplatinate precursor is not isolated at all and the pH of the reaction mixture is controlled by addition of KOH; see Experimental Section.

A reviewer suggested testing pure K_2PtI_4, prepared according to the method of Olsson,[14] as an alternative platinum source in order to clarify the metalation process. Reactions conducted with this compound under the same conditions but under nitrogen rather than standard atmosphere gave mixtures of the *trans*-configured complex **2a**, the cycloplatinated target compound **3a**, and large amounts of platinum metal. We conclude that our mixed-valent precursor described above represents the superior alternative.

The *trans*-configured complexes MX_2L_2 of palladium and platinum are considered intermediates in cyclometalation; for the case of palladium, prior experimental evidence has been obtained.[15,16] In order to get insight into the reaction pathway of the synthesis reported here, the alleged intermediate **(*S,S*)-2a** has been isolated and fully characterized: When the reaction was quenched after 30 min by partial evaporation of methanol from the solvent mixture, the *trans* complex precipitated. When this compound was redissolved in methanol/water and an additional equivalent of the primary amine was provided to promote C−H activation, it underwent cycloplatination to **(*S,S*)-**

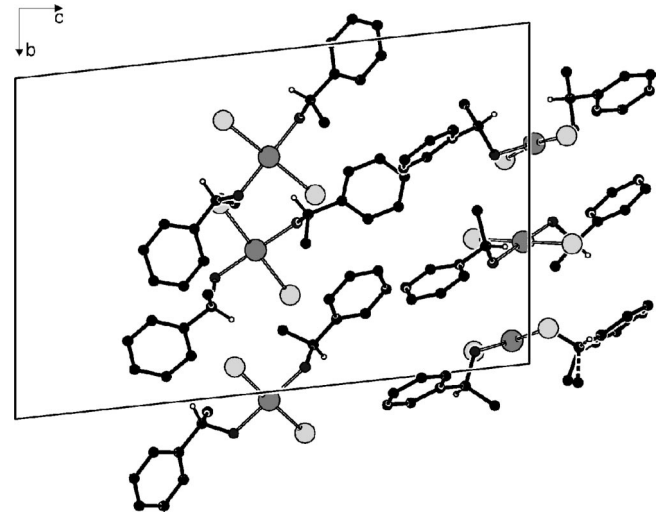


Figure 1. Arrangement of the six symmetrically independent molecules of **(*S,S*)-2a** in the unit cell. Pt−N min. 2.054(7) Å, max. 2.087(8) Å; Pt−I min. 2.6009(12) Å, max. 2.6199(11) Å; N−Pt−N min. 176.3(3)°, max. 178.8(3)°; I−Pt−I min. 171.88(3)°, max. 178.77(2)°; dihedral angles subtended by the plane of coordination and the phenyl rings min. 2.7(4)°, max. 26.2(4)°.

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Table 1. Experimental X-ray Diffraction Parameters and Crystal Data for 2a and the Cycloplatination Products α-3a, *β*-3a, and 3c

complex	(*S,S*)-2a	α-(*R,R*)-3a	*β*-(*S,S*)-3a	(*R,R*)-3c
empirical formula	$C_{16}H_{22}PtI_2N_2$	$C_{16}H_{21}PtIN_2$	$C_{16}H_{21}PtIN_2$	$C_{16}H_{19}PtF_2IN_2$
fw	691.25	563.33	563.33	599.32
cryst size (mm)	0.22 × 0.25 × 0.31	0.80 × 0.05 × 0.02	0.28 × 0.01 × 0.01	0.56 × 0.04 × 0.04
cryst habit, color	fragment, yellow	rod, light yellow	rod, light yellow	rod, colorless
cryst syst	triclinic	orthorhombic	monoclinic	orthorhombic
space group	*P*1	$P2_12_12_1$	$P2_1$	$P2_12_12_1$
a (Å)	9.908(3)	4.6146(3)	11.311(2)	4.5846(13)
b (Å)	14.267(4)	11.7364(8)	4.6196(9)	11.894(3)
c (Å)	21.596(5)	29.866(2)	15.981(3)	30.144(9)
α (deg)	96.105(5)			
β (deg)	91.797(5)		98.687(4)	
γ (deg)	92.448(5)			
V (Å^3)	3030.7(14)	1617.49(19)	825.5(3)	1643.7(8)
D (g·cm^{-1})	2.272	2.313	2.266	2.422
Z	6	4	2	4
T (K)	130(2)	100(2)	130(2)	130(2)
μ(Mo Kα) (mm^{-1})	9.997	10.576	10.362	10.432
F(000)	1896	1048	524	1112
θ range (deg)	2. 06−26.00	2.21−33.78	2.07−28.35	2.65−29.82
no. of reflns collected	52 490	52 872	11 167	14 555
R_{int}	0.0341	0.0626	0.0736	0.0836
no. of unique reflns in refin	23 702	6147	4030	4304
no. of reflns with $I > 2\sigma(I)$	22 576	5720	3594	3441
no. of params refined	1147	183	183	201
R_1 ($2\sigma(I)$)	0.0348	0.0301	0.0524	0.0453
R_1 (all data)	0.0371	0.0331	0.0600	0.0572
wR_2	0.0829	0.0616	0.0928	0.0750
Flack's param	0.007(3)	0.002(5)	0.029(11)	−0.009(9)
goodness of fit	1.027	1.070	1.018	1.001
diff peak/hole (e/Å^3)	1.27/−0.98	−1.09/2.13	−3.24/1.79	−0.46/0.97

3a within a few hours, in agreement with the concept of an intermediate.

(*S,S*)-2a, isolated as outlined above, was characterized by microanalysis and by spectroscopic methods. The ^{195}Pt chemical shift amounts to −3354 ppm; a recent review on ^{195}Pt spectroscopy reports a range between −3336 and −3372 ppm for the chemical shifts of *trans* diiodo platinum complexes of primary amines.[17] In addition, single crystals of **(*S,S*)-2a** were studied by X-ray diffraction: The compound is associated with a solid state structure of surprising[18] complexity, featuring six symmetrically independent square-planar, *trans*-configured molecules (Figure 1) that differ mainly with respect to conformation. Displacement ellipsoid plots of all independent molecules are provided in the Supporting Information (Figure S1).

Isolation of the *trans*-configured intermediate **(*S,S*)-2a**, albeit very possible, is not mandatory: As shown in Scheme 1, the primary amines **1a**−**c** can be directly converted into the corresponding *ortho*-platinated complexes **3a**−**c**. In addition to the unsubstituted 1-phenylethylamine **1a**, we deliberately decided to test the electron-rich *para* methyl derivative **1b** and its electron-deficient *para* fluoro congener **1c**: We recall that the more popular cyclopalladation was originally limited to electron-rich substrates.[1,3] Reaction times are longer for the fluoro derivative, but all three target complexes **3a**−**c** may be obtained in high yields. Best results are achieved using a slight excess of the amine (see Experimental Section), but a 3:1 molar ratio between amine and precursor is in principle sufficient. The products have been isolated and characterized by microanalysis and spectroscopic methods. In the cases of **3a** and **3c**, single crystals suitable for X-ray diffraction have been obtained; prior to these results, only one structural study on cycloplatinated benzylamine had been carried out.[7] From the metalation of enantiomerically pure **1a** two different polymorphs were encountered. One of these polymorphs, hereafter referred to as **α-3a**, crystallizes in the orthorhombic space group $P2_12_12_1$. The alternative modification ***β*-3a** exhibits roughly related lattice parameters (cf. Table 1) in the monoclinic space group $P2_1$ and slightly less efficient space filling. Figure 2 shows the molecular structures in both polymorphs. The most significant difference between molecules in **α-** and ***β*-3a** pertains to the rotation around the N−C bond in the monohapto amine ligand.

ortho-Platination is not restricted to 1-phenylethylamine **1a** but tolerates substitution in the *para* position of the aromatic ring of the primary amine. The conversion of the methyl-substituted and hence electron-rich **1b** to the cycloplatinated complex **3b** proceeds faster than for the unsubstituted phenylethylamine **1a**, whereas **1c**, due to its electron-withdrawing fluoro substituent, requires a prolonged reaction time to form **3c**. Very high yields confirm that our approach tolerates substitution on the aryl ring of the primary amine. All three complexes **3a**−**c** show ^{195}Pt resonances at ca. −3300 ppm, a rather high field for Pt(II) compounds in general but not surprising for organoplatinum compounds.[19] In the ^{13}C spectrum of **3c** the fluoro substitution is reflected in a characteristic chemical shift for the substituted carbon atom of ca. 160 ppm. Single-crystal X-ray diffraction proved that the fluoro derivative is isomorphous with the α-polymorph of **3a**: Both compounds crystallize in the same space group with very similar lattice pameters, and initial phases for the crystal structure of **3c** could be derived using the model of **3a**. The interatomic distance between the metal center and the nitrogen atom of the *ortho*-metalated ligand in compounds **3a** and **3c** is consistently shorter than the Pt−N bonds to the *σ* donor, although this difference is hardly significant at the level of an individual structure. The molecular structure of **3c** (Figure S2, Supporting Information)

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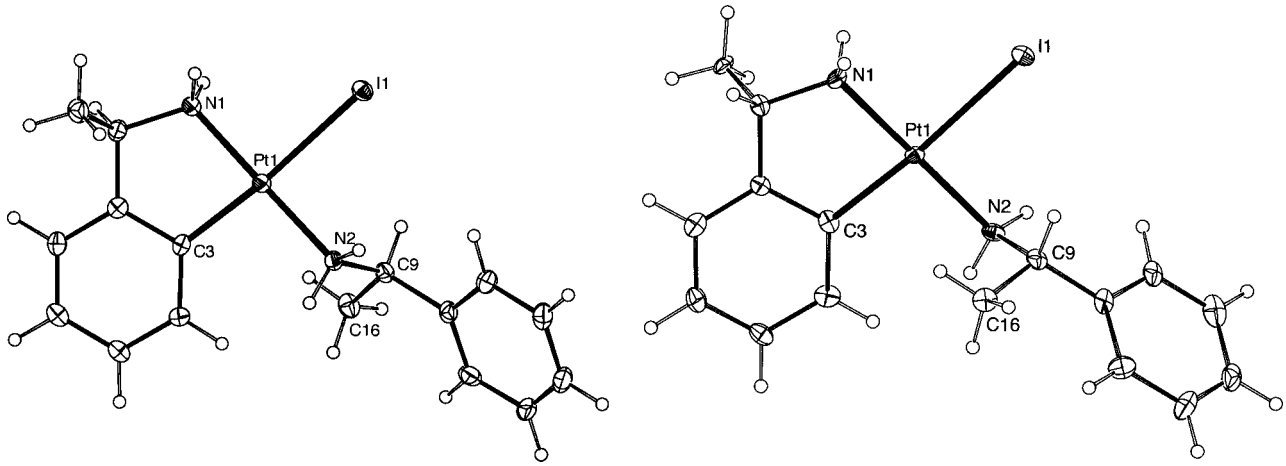

Figure 2. Molecular structures of **(*R,R*)-α-3a** (orthorhombic polymorph, left) and **(*S,S*)-*β*-3a** (monoclinic polymorph, right) in the solid. Displacement ellipsoids are drawn at 30% probability; H atoms are shown with arbitrary radius. Selected interatomic distances (Å) and angles (deg) for **(*R,R*)-α-3a** [values for **(*S,S*)-*β*-3a** in square brackets]: Pt1−N1 2.034(4) [2.062(10)], Pt1−N2 2.058(4) [2.067(10)], Pt1−I1 2.6966(3) [2.7075(10)], Pt1−C3 1.999(4) [2.003(12)], N1−Pt1−N2 179.16(16) [177.6(4)], C3−Pt1−I1 174.93(13) [174.7(3)], N1−Pt1−I1 91.71(10) [91.8(3)], N2−Pt1−I1 87.83(10) [88.2(3)], C3−Pt1−N1 83.22(17) [83.1(5)], C3−Pt1−N2 97.23(17) [96.8(4)]; Pt1−N2−C9−C16 −71.5(4) [−65.1(12)].

closely matches that of its unsubstituted congener, and differences are limited to soft intramolecular degrees of conformation.

So far we have discussed the reaction sequence of primary amines **1** either directly or via the intermediate *trans* complexes **2** to organoplatinum derivatives **3**. These complexes exhibit the same amine as a chelating *ortho*-metalated and a monodentate ligand. The latter moiety may be substituted by a variety of donor ligands; thus, a wide spectrum of cycloplatinated primary amines becomes accessible. Two classes of substitution products have been characterized in the context of this work, namely, the phosphane complex **4a** and the pyridine derivatives **5a**−**c**. When **3a** is stirred in CH_2Cl_2 at room temperature with triphenylphosphane, the monohapto primary amine is replaced in a relatively fast reaction and product **4a** was isolated in high yield by precipitation with hexane. X-ray diffraction revealed that the bulky triphenylphosphane ligand in **(*S*)-4a** leads to a significant distortion in the idealized square-planar coordination of the metal center: the angle C21−Pt1−I1 (Figure 3) amounts to 165.54(15)° and is by far the smallest *trans* angle in all structures reported in this work.

Not only in **3a**, the cycloplatination product of the unsubstituted amine, but also in the *para*-substituted derivatives **3b** and **3c** may the monohapto amines be replaced by alternative ligands. In addition to phosphanes as shown above, N-donor ligands such as pyridine derivatives may be employed. The reactions of **3a**−**c** with 4-picoline are slow, even at elevated temperatures. In the case of **3b**, NMR control at regular intervals revealed that the reaction in benzene at 65 °C was complete after 3 days. The substitution of the monodentate amine in **3c** is faster and requires 24 h in refluxing methanol. All three substitution products **5a**−**c** have been isolated and characterized, and we have been able to obtain single crystals suitable for X-ray diffraction studies. **5a**−**c** are isomorphous, crystallizing in the tetragonal space group $I4_1$ with two independent molecules in the asymmetric unit: Their displacement ellipsoid plots are reported in Figure 4 and in the Supporting Information, Figures S3 and S4. These graphical representations of the symmetrically independent pairs also allow one to appreciate the pseudosymmetry in the structures, cf. Experimental Section. We had

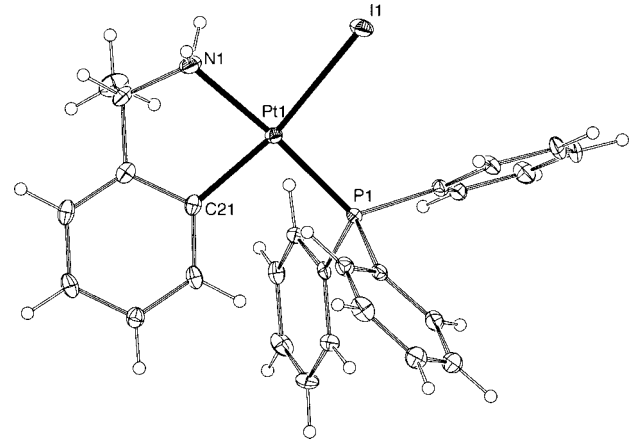

Figure 3. Molecular structure of **(*S*)-4a** in the crystal. Displacement ellipsoids are drawn at 30% probability; H atoms are shown with arbitrary radius. Selected interatomic distances (Å) and angles (deg): Pt1−N1 2.108(5), Pt1−P1 2.2338(14), Pt1−I1 2.7008(5), Pt1−C21 2.041(6), N1−Pt1−P1 172.43(15), C21−Pt1−I1 165.55(15), N1−Pt1−I1 87.85(14), P1−Pt1−I1 97.42(4), C21−Pt1−N1 81.1(2), C21−Pt1−P1 −94.54(16).

encountered a closely related structure for (*R*)-PdCl(C_6H_4-CHMeNH_2)(pyridine) in the context of cyclopalladation.[20]

In agreement with our expectation and the prior examples for cycloplatinated tertiary amines compiled in the CSD,[8] the metal−carbon bond represents the shortest in the coordination sphere. With respect to the iodo substituents, the crystal structures communicated in this work feature 22 symmetrically independent Pt−I bonds. These interatomic distances reflect the influence of the ligand in *trans* position. When the *trans* ligand is a second iodo substituent as in **2a**, Pt−I falls in the range between 2.6009(12) and 2.6199(11) Å, whereas longer Pt−I bonds (min. 2.6814(15) Å) are observed for all the other compounds with C-bonded ligands in *trans* position. In **3c**, with the electron-deficient chelating amine, the Pt−I distance amounts to 2.6878(10) Å and is shorter than in both polymorphs of **3a**, the unsubstituted cycloplatinated amine, where values of

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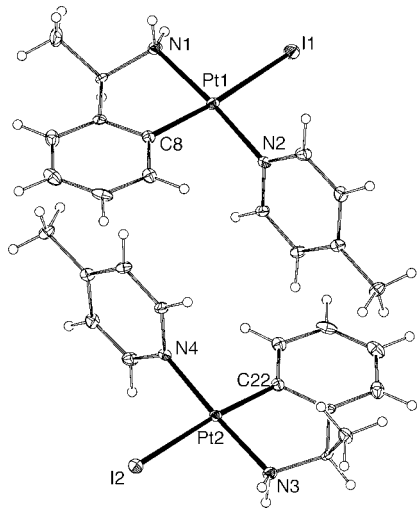


Figure 4. Molecular structures of the two independent molecules of **(*R*)-5a** in the crystal. Displacement ellipsoids are drawn at 30% probability; H atoms are shown with arbitrary radius. Selected interatomic distances (Å) and angles (deg) [values for the second molecule in square brackets]: Pt1−N1 2.056(13), [2.005(13)], Pt1−N2 2.011(12), [2.024(12)], Pt1−I1 2.6814(15), [2.6912(14)], Pt1−C8 2.010(15), [1.954(15)], N2−Pt1−N1 175.3(5), [176.1(5)], C8−Pt1−I1 174.2(4), [174.7(4)], N1−Pt1−I1 93.3(4), [93.2(4)], N2−Pt1−I1 91.2(4), [90.6(4)], C8−Pt1−N1 80.9(5), [81.5(6)], N2−Pt1−C8 94.6(6), [94.7(6)]. Dihedral angle between plane of coordination and pyridine ring: 73.0(5) [82.7(5)].

2.6966(3) and 2.7075(10) Å are encountered. No reliable trend can be deduced for the less accurate structures **5a**−**c**.

A short discussion of the intermolecular aspects in the crystal structures is appropriate: The primary amines represent good donors for classical hydrogen bonds; however, in the absence of suitable acceptors other than iodide not all N−H groups can participate in efficient hydrogen bonding. The aryl-bonded fluorine in **3c** and **5c** does not accept any classical hydrogen bond. Shortest interhalide contacts occur in **2a** with I···I distances of ca. 4.3 Å, and closest intermetal contacts of ca. 3.9−4.0 Å are observed in **5a**−**c**.

Concluding Remarks

In this contribution we have reported a convenient and general access to cycloplatinated primary amines. As the organoplatinum complexes directly obtained by this reaction can undergo substitution with suitable donor ligands, this approach will pave the way to a wide range of compounds. The nature of the iodoplatinate precursor represents an important issue for future investigation. Furthermore, we intend to study the cytotoxicity of cycloplatinated primary amines.

Experimental Section

General Comments. NMR spectra were recorded on a Varian Mercury 200 (^{19}F NMR: 188.15 MHz), a Varian Mercury 300 (^{31}P: 121.45 MHz), a Varian Unity 500 (^{1}H: 500 MHz, ^{13}C: 125 MHz, ^{195}Pt: 107.4 MHz), and a Bruker Avance II (^{1}H: 400 MHz, ^{13}C: 100 MHz, ^{19}F: 376.5 MHz) at ambient temperature. ^{1}H and ^{13}C resonances are referenced to TMS, ^{19}F spectra to CCl_3F, ^{31}P to H_3PO_4, and ^{195}Pt to H_2PtCl_6. Yields refer to the initial amount of platinum introduced into the reaction.

Preparation of the Iodoplatinate Precursor. K_2PtCl_4 (500 mg, 1.2 mmol) was dissolved in 5 mL of H_2O. Then 0.63 mL (4.8 mmol) of 57% hydroiodic acid was added to the solution, and the mixture was stirred at room temperature for 2 h. Evaporation of the water resulted in black K_2PtI_x, which was recovered in quantitative yield. Preparation of the precursor may be achieved within much shorter reaction times, e.g., 10 min, albeit at the expense of lower yields in the subsequent cycloplatination reaction.

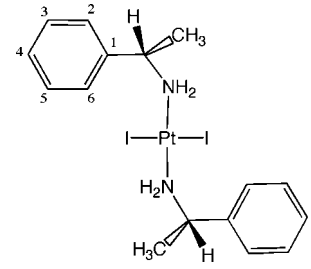
Cycloplatination. A 1.2 mmol amount of K_2PtI_x prepared as above was suspended in 30 mL of MeOH/H_2O (2:1). Then 4.8 mmol of ligand **1** was added, and the reaction mixture was heated to reflux. The color of the reaction mixture changed from dark brown via yellow to almost colorless, and a white precipitate formed. This solid was recovered by filtration and washed with 20 mL of cold MeOH/H_2O (2:1). Reaction times: For **1a** *ortho*-platination 4 h, for **1b** less than 3 h, and for **1c** ca. 1 day. The intermediate product **2a** was isolated and characterized. This complex may be precipitated after a reaction time of ca. 30 min by addition of water or by concentration of the reaction mixture as a yellow crystalline solid. Yields: 96% (1.152 mmol) for **2a**, 86% (1.032 mmol) for **3a**, 87.5% (1.05 mmol) for **3b**, and 86% (1.032 mmol) for **3c**. The difference between the yields and the quantitative yield represents mostly the *trans*-PtI_2L_2 precursor, a product that could be isolated and used for further *ortho*-platination.

Cycloplatination without Isolation of the Precursor. K_2PtCl_4 (500 mg, 1.2 mmol) was dissolved in 5 mL of H_2O. Then 0.63 mL (4.8 mmol) of 57% hydroiodic acid was added to the solution, and the mixture was stirred at room temperature for 2 h. At this point 20 mL of MeOH and 5 mL of H_2O were added, and the pH of the reaction mixture was adjusted to a value of ca. 2.5 using drops of a solution of KOH in MeOH/H_2O (2:1). Ligand **1a** (4.8 mmol) was added, and the reaction mixture was heated to reflux for 4 h. The white precipitate formed was recovered by filtration and washed with 20 mL of cold MeOH/H_2O (2:1). Yield: 82% (0.984 mmol) for **3a**.

Substitution Reactions. 4a. 3a (0.5 mmol, 0.282 g) was disolved in 10 mL of CH_2Cl_2 at room temperature, and an equimolar amount of PPh_3 (0.131 g) was added. After 4 h the clear reaction mixture was concentrated, and **4a** was precipitated as a white powder by adition of hexane. Yield: 93% (1.116 mmol).

5a, 5b, 5c. A 0.5 mmol amount of the cycloplatinated amine **3a** (0.282 g), **3b** (0.296 g), and **3c** (0.300 g) was dissolved in 15 mL of CH_2Cl_2. An equimolar amount of 4-picoline (0.0465 g) was added, and the reaction mixture was heated to reflux for 2 days. The white precipitate formed was filtered off. Yield: 88% (1.056 mmol) for **5a**, 79% (0.948 mmol) for **5b**, and 82% (0.984 mmol) for **5c**.

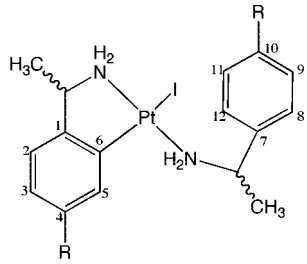
Spectroscopic and Analytical Results. 2a: *trans*-(*S*,*S*)-PtI-($C_6H_5CHMeNH_2$)($H_2NCHMeC_6H_5$). NMR. ^{1}H NMR (400



2a

MHz, CD_2Cl_2): δ 1.71 (d, 6H, J = 6.92 Hz, CH*Me*); 3.50−3.90 (br, 4H, N*H*$_2$); 4.50 (m, 2H, C*H*Me); 7.29−7.40 (m, 10H, *H*$_2$−*H*$_6$) ppm. ^{13}C NMR (100.6 MHz, CD_2Cl_2): δ 21.60 (s, 2C, *C*H$_3$); 57.79 (s, 2C, *C*H); 127.71, 128.27 (s, 10C, *C*$_2$−*C*$_6$), 141.32 (s, 2C, *C*$_1$) ppm. ^{195}Pt NMR (107.4 MHz, CD_2Cl_2): δ −3354.21 ppm. Anal. Calcd for $C_{16}H_{22}PtI_2N_2$: H: 3.21, C: 27.80, N: 4.05. Found: H: 3.19, C: 27.79, N: 4.02. Mp: 149 °C.

3a, 3b, 3c:. (*S*,*S*)- or (*R*,*R*)-PtI(4-R-$C_6H_4CHMeNH_2$)(H_2-$NCHMeC_6H_5$-4-R). 3a. NMR. ^{1}H NMR (400 MHz, C_6D_6): δ 0.93 (d, 3H, J = 6.56 Hz, CH*Me* cycloplatinated amine); 1.58



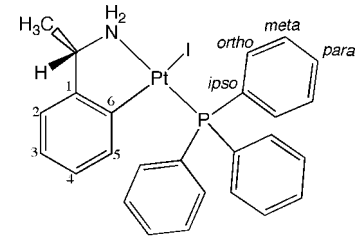
3a (R = H), **3b** (R = CH_3), **3c** (R = F)

(d, 3H, J = 6.80 Hz, CH*Me* noncycloplatinated amine); 3.09, 3.44 (br, 2H, NH_2, noncycloplatinated amine); 3.26, 5.23 (br, 2H, NH_2, cycloplatinated amine); 3.74 (m, 1H, C*H*, cycloplatinated amine); 4.13 (m, 1H, C*H*, noncycloplatinated amine); 6.63, 6.74 (m, 2H, H_4, H_5); 6.64, 6.66 (m, 2H, H_2, H_3); 6.86 (m, 1H, H_{10}); 7.02 (m, 2H, H_8, H_{12}); 7.03 (m, 2H, H_9, H_{11}) ppm. ^{13}C NMR (100.6 MHz, C_6D_6): δ 23.00 (s, 1C, *C*H_3, noncycloplatinated amine); 24.06 (s, 1C, *C*H_3, cycloplatinated amine); 58.39 (s, 1C, *C*H, noncycloplatinated amine); 62.96 (s, 1C, *C*H, cycloplatinated amine); 121.22, 128.19 (s, 2C, C_4, C_5); 123.64, 125.22 (s, 2C, C_2, C_3); 126.36 (s, 1C, C_{10}); 127.92 (s, 2C, C_8, C_{12}); 128.46 (s, 2C, C_9, C_{11}); 139.81 (s, 1C, C_6); 143.18 (s, 1C, C_7); 155.20 (s, 1C, C_1) ppm. ^{195}Pt NMR (107.4 MHz, C_6D_6): δ −3302.81 ppm. Anal. Calcd for $C_{16}H_{21}PtIN_2$: H: 3.76, C: 34.11, N: 4.97. Found: H: 3.72, C: 34.29, N: 5.02. Mp: 199 °C.

3b. NMR. ^{1}H NMR (400 MHz, C_6D_6): δ 0.99 (d, 3H, J = 6.60 Hz, CH*Me* cycloplatinated amine); 1.60 (d, 3H, J = 6.76 Hz, CH*Me* noncycloplatinated amine); 1.87 (s, 3H, 4-*Me*(Ph) cycloplatinated amine); 2.09 (s, 3H, 4-*Me*(Ph) noncycloplatinated amine); 2.61 (br, 1H, N*H*, noncycloplatinated amine); 3.35 (br, 2H, N*H* noncycloplatinated and N*H* cycloplatinated amines); 4.00 (m, 2H, C*H*, noncycloplatinated and cycloplatinated amines); 6.06 (br, 1H, N*H*, cycloplatinated amine); 6.39 (s, 1H, H_5); 6.42 (d, 1H, J = 7.60 Hz, H_3); 6.61 (d, 1H, J = 7.56 Hz, H_2); 6.69 (d, 2H, J = 8.00 Hz, H_8, H_{12}); 6.87 (d, 2H, J = 7.80 Hz, H_9, H_{11}) ppm. ^{13}C NMR (100.6 MHz, C_6D_6): δ 21.08 (s, 2C, 4-*C*H_3(Ph), noncycloplatinated and cycloplatinated amines); 23.45 (s, 1C, *C*H_3, noncycloplatinated amine); 24.65 (s, 1C, *C*H_3, cycloplatinated amine) 58.53 (s, 1C, *C*H, noncycloplatinated amine); 62.57 (s, 1C, *C*H, cycloplatinated amine); 120.63, (s, 1C, C_2); 124.34 (s, 1C, C_3); 126.15 (s, 2C, C_8, C_{12}); 129.54 (s, 1C, C_5); 129.68 (s, 2C, C_9, C_{11}); 133.91 (s, 1C, C_4); 137.70 (s, 1C, C_{10}); 140.00 (s, 1C, C_6); 141.00 (s, 1C, C_7); 153.11 (s, 1C, C_1) ppm. ^{195}Pt NMR (107.4 MHz, C_6D_6): δ −3297.59 ppm. Anal. Calcd for $C_{18}H_{25}PtIN_2$: H: 4.26, C: 36.56, N: 4.74. Found: H: 4.30, C: 35.77, N: 4.65.

3c. NMR. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 1.46 (d, 3H, J = 6.60 Hz, CH*Me* cycloplatinated amine); 1.60 (d, 3H, J = 6.59 Hz, CH*Me* noncycloplatinated amine); 3.64 (br, 2H, N*H* noncycloplatinated and N*H* cycloplatinated amines); 3.79 (br, 2H, N*H* amine noncycloplatinated amine); 4.24 (m, 1H, C*H*, cycloplatinated amines); 4.46 (m, 1H, C*H*, noncycloplatinated amines); 4.64 (br, 1H, N*H*, amine, cycloplatinated amine); 6.36 (s, 1H, H_5); 6.66 (m, 1H, H_3); 6.91 (m, 1H, H_2); 7.09 (m, 2H, H_8, H_{12}); 7.38 (m, 2H, H_9, H_{11}) ppm. ^{13}C NMR (100.6 MHz, CD_2Cl_2): δ 22.91 (s, 1C, *C*H_3, noncycloplatinated amine); 24.25 (s, 1C, *C*H_3, cycloplatinated amine) 57.98 (s, 1C, *C*H, noncycloplatinated amine); 62.89 (s, 1C, *C*H, cycloplatinated amine); 110.22, (d, 1C, J_{C-F} = 21.40 Hz, C_3); 114.79 (d, 1C, J_{C-F} = 18.72 Hz, C_5); 116.27 (d, 2C, J_{C-F} = 20.06 Hz, C_8, C_{12}); 122.83 (d, 1C, J_{C-F} = 8.03 Hz, C_2); 128.78 (d, 2C, J_{C-F} = 7.46 Hz, C_9, C_{11}); 138.66 (s, 1C, C_7); 141.84 (s, 1C, C_6); 149.82 (s, 1C, C_1); 160.20 (d, 1C, J_{C-F} = 246.53 Hz, C_4); 163.04 (d, 1C, J_{C-F} = 246.53, C_{10}) ppm. ^{19}F NMR (376,3 MHz, CD_2Cl_2): δ−114.07 (m, 1F, noncycloplatinated amine); −116.70 (m, 1F, cycloplatinated amine). ^{195}Pt NMR (107.4 MHz, CD_2Cl_2): −3315.87 ppm. Anal. Calcd for $C_{16}H_{19}PtF_2IN_2$: H: 3.20, C: 32.07, N: 4.67. Found: H: 3.30, C: 31.99, N: 4.61. Mp: 223 °C with decomposition.

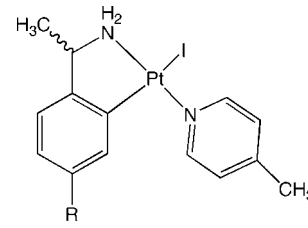
4a: (*S*)-PtI(4-R-C_6H_4CHMeNH_2)(PPh_3). NMR. ^{1}H NMR



4a

(400 MHz, CD_2Cl_2): δ 1.59 (d, 3H, J = 6.84 Hz, CH*Me*); 4.38 (q, 1H, J = 5.12 Hz, C*H*); 5.29 (br, 1H, N*H*); 6.04 (br, 1H, N*H*); 6.24 (m, 1H, *Ph*); 6.38 (dd, 1H, J = 2.80 Hz, J = 7.74 Hz, *Ph*); 6.77 (m, 1H, *Ph*); 6.94 (m, 1H, *Ph*); 7.39−7.45 (m, 9H, PPh_3); 7.63−7.70 (m, 6H, PPh_3) ppm. ^{13}C NMR (100.6 MHz, CD_2Cl_2): δ = 25.14 (s, 1C, *C*H_3); 62.67 (s, 1C, *C*H); 121.10, (s, 1C, *Ph*); 122.66 (s, 1C, *Ph*); 124.33 (s, 2C, *Ph*); 127.71 (d, 6C, J_{C-P} = 10.06 Hz, *meta-C,* PPh_3); 130.39 (s, 3C, *para-C,* PPh_3); 134.64 (d, 6C, J_{C-P} = 10.06 Hz, *ortho-C,* PPh_3); 132.02 (d, 3C, J_{C-P} = 57.35 Hz, *ipso-C,* PPh_3); 142.48 (s, 1C, C_6); 155.65 (s, 1C, C_1) ppm. ^{31}P NMR (121.45 MHz,CD_2Cl_2): δ 21.66 (t, 1P, J_{P-Pt} = 4421.78 Hz, *P*Ph$_3$). ^{195}Pt NMR (107.4 MHz, DMSO): −4253.82 (d, 1Pt, J_{P-Pt} = 4043.15) ppm. Anal. Calcd for $C_{26}H_{25}PtINP$: H: 3.58, C: 44.33, N: 1.99. Found: H: 3.68, C: 44.54, N: 2.00. Mp: 249 °C with decomposition.

5a, 5b, 5c: (*S*)- or (*R*)-PtI(4-R-C_6H_4CHMeNH_2)(4-picoline). 5a. NMR. ^{1}H NMR (400 MHz, C_6D_6): δ 0.82 (d, 3H,



5a (R = H), **5b** (R = CH_3), **5c** (R = F)

J = 6.60 Hz, CH*Me* cycloplatinated amine), 1.40 (s, 1H, 4-*Me*(Py)); 3.40- 3.60 (b, 2H, NH_2); 4.19 (m, 1H, C*H*); 6.00−8.76 (m, 7H, *Ph, Py*) ppm. ^{195}Pt NMR (107.4 MHz, C_6D_6): δ −3306.29 (s, 1Pt) ppm. Anal. Calcd for $C_{14}H_{17}PtIN_2$: H: 3.20, C: 31.41, N: 5.23. Found: H: 3.29, C: 32.31, N: 5.35. Mp: 241 °C with decomposition.

5b. NMR. ^{1}H NMR (400 MHz, C_6D_6): δ 0.88 (d, 3H, J = 6.60 Hz, CH*Me* cycloplatinated amine), 1.53 (s, 1H, CH*Me*), 2.09 (s, 1H, 4-*Me*(Py)); 3.05, 3.59 (m, 2H, NH_2); 4.08 (m, 1H, C*H*); 6.02−8.38 (m, 7H, *Ph, Py*) ppm. ^{195}Pt NMR (107.4 MHz, C_6D_6): δ −3188.05 (s, 1Pt) ppm. Anal. Calcd for $C_{15}H_{19}PtIN_2$: H: 3.49, C: 32.80, N: 5.10. Found: H: 3.61, C: 32.77, N: 4.99. Mp: 218 °C with decomposition.

5c. NMR. ^{1}H NMR (400 MHz, C_6D_6): δ 1.32, 1.34 (s, 2H, CH*Me,* 4-*Me*(Py)); 2.63, 2.97 (m, 2H, NH_2); 4.28 (m, 1H, C*H*); 6.59−6.69 (m, 7H, *Ph, Py*) ppm. ^{19}F NMR (188.15 Mhz, C_6D_6): δ −113.32 (m, 1F, F) ppm. ^{195}Pt NMR (107.4 MHz, C_6D_6): δ −3376.38 (s, 1Pt) ppm. Anal. Calcd for $C_{14}H_{16}PtFIN_2$: H: 2.91, C: 30.39, N: 5.06. Found: H: 3.01, C: 30.10, N: 4.98.

Single-Crystal X-ray Diffraction. Suitable crystals for X-ray diffraction were obtained by slow evaporation of 2-propanol/

Table 2. Experimental X-ray Diffraction Parameters and Crystal Data for the Substitution Products 4a and 5a−c

complex	(*S*)-**4a**	(*R*)-**5a**	(*S*)-**5b**	(*S*)-**5c**
empirical formula	$C_{26}H_{25}PtINP$	$C_{14}H_{17}PtIN_2$	$C_{15}H_{19}PtIN_2$	$C_{14}H_{16}PtFIN_2$
fw	704.42	535.29	549.31	553.28
cryst size (mm)	0.47 × 0.14 × 0.03	0.19 × 0.09 × 0.04	0.21 × 0.04 × 0.04	0.30 × 0.10 × 0.10
cryst habit, color	rod, light yellow	rod, colorless	fragment, colorless	fragment,light yellow
cryst syst	monoclinic	tetragonal	tetragonal	tetragonal
space group	$P2_1$	$I4_1$	$I4_1$	$I4_1$
a (Å)	9.975(2)	19.0287(5)	18.990(3)	19.091(3)
b (Å)	8.3934(19)			
c (Å)	14.854(3)	16.3448(10)	17.965(6)	16.950(3)
β (deg)	104.246(4)			
V (Å^3)	1205.4(4)	5918.3(4)	6478(2)	6177.7(16)
D (g·cm^{-1})	1.941	2.403	2.253	2.379
Z	2	16	16	16
T (K)	130(2)	100(2)	100(2)	130(2)
μ(Mo Kα) (mm^{-1})	7.180	11.555	10.559	11.083
F(000)	668	3936	4064	4064
θ range (deg)	2.11−28.33	1.51−28.26	1.52−28.61	1.51−26.00
no. of reflns collected	16 539	10 303	10 559	36 320
R_{int}	0.0399	0.0284	0.0800	0.0480
no. of unique reflns in refin	5956	7188	7493	6080
no. of reflns with $I > 2\sigma(I)$	5657	5915	5003	5370
no. of params refined	272	239	253	239
R_1 ($2\sigma(I)$)	0.0322	0.0376	0.0540	0.0311
R_1 (all data)	0.0343	0.0506	0.1033	0.0367
wR_2	0.0788	0.0804	0.1101	0.0782
Flack's param	−0.010(5)	0.042(18)	0.07(3)	0.053(17)
goodness of fit	1.018	1.072	0.993	1.005
diff peak/hole (e/Å^3)	−1.21/2.17	−1.14/1.32	−1.20/2.13	−1.12/2.17

CH_2Cl_2 solutions at room temperature. Crystal data, parameters for intensity data collection, and convergence results are compiled in Table 1 (for the intermediate **2a** and the direct products of cycloplatination, **α-3a**, ***β*-3a**, **3c**) and Table 2 (for the substitution products **4a**, **5a−c**). Data were collected with Mo Kα radiation (graphite monochromator, $\lambda = 0.71073$ Å) on a Bruker D8 goniometer with a SMART APEX CCD area detector. An analytical absorption correction[21,22] based on face-indexing was performed for the well-shaped crystal of **3c**, whereas in the other cases multiscan absorption corrections were applied by SADABS[23] or PLATON.[22] Unit cell parameters were obtained by least-squares refinement of up to 9999 reflections. The structures were solved by direct methods (SHELXS-97)[24] and refined by full matrix least-squares procedures based on F^2 with all measured reflections (SHELXL-97).[25] Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were introduced in calculated positions (dC−H = 0.98 Å, dN−H = 0.95 Å) and refined using a riding model. The absolute configurations of the enantiomerically pure reagents were confirmed by evaluation of the Flack[26] parameter. The crystal structures of **5a−c** are isomorphous and show pronounced pseudosymmetry with strong correlation between parameters for atoms in symmetrically independent molecules related by pseudoinversion. Displacement parameters within each atom pair were constrained to be equal, and distance restraints were applied in order to ensure physically meaningful results and convergence. Nevertheless, it has to be noted that the inherent pseudosymmetry affects the accuracy of these structures. We will attempt to perform nonroutine diffraction experiments at high resolution, possibly for one of the cycloplatinated amines **3a** or **3c** not affected by pseudosymmetry, in order to obtain more precise geometry parameters for the molecular structure of a primary amine. Crystallographic data for all structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-681252 (for **2a**), 677332 (for **α-3a**), 681253 (for ***β*-3a**), 681254 (for **3c**), 681255 (for **4a**), 677333 (for **5a**), 681256 (for ***5β***), and 681257 (for **5c**).

Acknowledgment. The authors thank Manuel Krott for help with powder diffraction, Toni Gossen for ^{195}Pt NMR spectra, and an anonymous referee for helpful comments.

Supporting Information Available: Crystallographic information for all structures in CIF format; refinement details and displacement ellipsoid plots for the six independent molecules in (***S,S*)-2a**, displacement ellipsod plots of (***R,R*)-3c**, (*S*)-**5b**, and (*S*)-**5c** in the solid state. This material is available free of charge via the Internet at http://pubs.acs.org.

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