Organometallics in Water: Three-Coordinate [Pt^0(N,N-chelate)(η^2-olefin)] Complexes Containing New Chiral Ligands Based on α-D-Mannose

Maria L. Ferrara, Ida Orabona, and Francesco Ruffo*

Dipartimento di Chimica, Università di Napoli "Federico II", via Mezzocannone 4, I-80134 Napoli, Italy

Maria Funicello

Dipartimento di Chimica, Università della Basilicata, via Nazario Sauro 85, I-85100 Potenza, Italy

Achille Panunzi

Facoltà di Agraria and Dipartimento di Chimica, Università di Napoli "Federico II", via Mezzocannone 4, I-80134 Napoli, Italy

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Summary: New bidentate nitrogen ligands based on α*-D-mannose were prepared and investigated by preparing a family of platinum(0) complexes of formula [Pt(N,N-chelate)(*η^2*-olefin)]. The ability of one N,N-chelate to induce a stereoselective reaction in water was assessed.*

The design of environmentally "friendly" processes plays a prominent role in contemporary chemistry. A plausible approach to the problem involves the extension to aqueous media of the processes now performed in organic solvents.[1] With reactions promoted by metals, the ancillary ligands should (i) confer solubility in water, (ii) be economically affordable, and (iii) possibly display chirality. On this basis, we undertook the synthesis of new N,N-bidentate ligands possessing the aforementioned requirements. With the assumption that natural products are often readily accessible as well as generally chiral, we decided to examine derivatives of the easily available carbohydrate α-D-mannose.[2] An attractive feature of this type of ligand is the possibility of either lipophilic or hydrophilic behavior, depending on whether the alcoholic functions in the sugar residues are protected.

In this report we describe preliminary results dealing with the synthesis of new ligands and their use in preparing a series of organometallic platinum(0) complexes of formula [Pt(N,N-chelate)(η^2-olefin)].

The chemistry developed in this work is depicted in Scheme 1, and a list of the new complexes is provided in Table 1. Our effort was initially directed toward the synthesis of protected ligands **1** and **2**, which are expected to display a fair solubility in common organic solvents. With the commercial precursor methyl-α-D-mannoside as starting material, a known procedure allowed the synthesis of azide **3**.[3] Addition of PMe_2Ph to **3** gave the iminophosphorane **4**[4,5] (path i), which in turn was converted into *N,N*-diimines **1**[6] and **2** by condensation with 6-methyl-2-pyridinecarboxaldehyde and glyoxal, respectively (ii and iii). Both **1** and **2** are readily soluble in organic solvents. They were coordinated to {Pt^0(η^2-olefin)} fragments by reaction with [Pt(η^2-norbornene)$_3$][7] in the presence of diphenyl or dimethyl fumarate (iv).[8] The corresponding complexes [Pt(**1**)(η^2-(*E*)-R″O$_2$CCH=CHCO$_2$R″)] and [Pt(**2**)(η^2-(*E*)-R″O$_2$CCH=CHCO$_2$R″)] could be isolated in high yield as orange-red microcrystalline solids. The analogous

(1) For recent examples, see: (a) Nait Ajjou, A.; Alper, H. *J. Am. Chem. Soc.* **1998**, *120*, 1466. (b) Lynn, D. M.; Mohr, B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1998**, *120*, 1627.

(2) Ligands based on carbohydrates are known. For recent examples, see: (a) Tanase, T.; Yasuda, Y.; Onaka, T.; Yano, S. *J. Chem. Soc., Dalton Trans.* **1998**, 345 and references therein. (b) Stolmar, M.; Floriani, C.; Gervasio, G.; Viterbo, D. *J. Chem. Soc., Dalton Trans.* **1997**, 1119. (c) Tschoerner, M.; Trabesinger, G.; Albinati, A.; Pregosin, P. S. *Organometallics* **1997**, *16*, 3447.

(3) Horton, D.; Luetzow, A. E. *Carbohydr. Res.* **1968**, *7*, 101.

(4) Compounds similar to **4** are known. For a recent example, see: Garcìa Fernàndez, J. M.; Mellet Ortiz, C.; Dìaz Pèrez, V. M.; Fuentes, J.; Kovàcs, J.; Pintèr, I. *Tetrahedron Lett.* **1997**, *38*, 4161.

(5) Synthesis of **4**: to a stirred solution of $PPhMe_2$ (0.14 g, 1.0 mmol) in 5 mL of dry dichloromethane kept in an ice bath was added dropwise a solution of **3** (0.42 g, 1.0 mmol) in 5 mL of dry dichloromethane. After the addition was complete, the ice bath was removed and formation of nitrogen was observed. After 10 h of stirring removal of the solvent under vacuum afforded the product as a white glassy solid in quantitative yield. Selected ^{1}H NMR resonances [in $CDCl_3$, $CHCl_3$ (δ 7.26) as internal standard, at 250 MHz, δ]: 5.48 (m, 2H), 5.27 (m, 1H), 4.70 (d, 1H), 3.95 (m, 1H), 3.41 (s, 3H, OMe), 3.3−3.1 (m, 2H), 2.13 (s, 3H, $MeCO_2$), 1.85 (s, 3H, $MeCO_2$), 1.60 [d, 3H, PPh(*Me*)Me′], 1.56 [d, 3H, PPh(Me)*Me*′]. Selected ^{13}C NMR resonances [in $CDCl_3$, $CDCl_3$ (δ 77) as internal standard, at 62.9 MHz, δ]: 98.3 (1C, C1 of mannoside), 73.5, 70.1, 69.7, and 68.8 (4C, C2−C5 of mannoside), 55.0 (1C, OMe), 46.7 (1C, NCH_2), 20.9 (1C, *Me*CO_2), 20.6 (1C, *Me*CO_2), 15.9 [$^1J_{P-C}$ = 21 Hz, PPh(*Me*)Me′], 14.8 [$^1J_{P-C}$ = 15 Hz, PPh(Me)*Me*′].

(6) Synthesis of **1**: to a solution of **4** (1.0 g, 2.0 mmol) in 5 mL of dry toluene containing A4 molecular sieves was added a solution of 6-methyl-2-pyridinecarboxaldehyde (0.24 *g*, 2.0 mmol) in 3 mL of dry toluene. After 1 h of stirring at 363 K the solvent was removed under vacuum. The residue was filtered through a column of Florisil (15 × 1.5 cm) with 1:1 petroleum ether/ethyl acetate to give the product as a light yellow glassy solid (0.80 g, yield 80%). $[\alpha]^{298} = +50°$. Selected ^{1}H NMR resonances [in $CDCl_3$, $CHCl_3$ (δ 7.26) as internal standard, at 200 MHz, δ]: 8.36 (s, 1H, CH=N), 5.60 (d, 2H), 5.31 (narrow m, 1H), 4.81 (narrow m, 1H), 4.29 (m, 1H), 3.96 (d, 1H), 3.75 (dd, 1H), 3.35 (s, 3H, OMe), 2.55 (s, 3H, Me-py), 2.15 (s, 3H, $MeCO_2$), 1.89 (s, 3H, $MeCO_2$). Selected ^{13}C NMR resonances [in $CDCl_3$, $CDCl_3$ (δ 77) as internal standard, at 50.3 MHz, δ]: 164.8 (1C, CH=N), 98.3 (1C, C1 of mannoside), 69.8, 69.7, 69.2, and 68.7 (4C, C2−C5 of mannoside), 61.6 (1C, NCH_2), 55.0 (1C, OMe), 24.3 (1C, *Me*-py), 20.9 (1C, *Me*CO_2), 20.7 (1C, *Me*CO_2). Anal. Calcd for $C_{25}H_{28}N_2O_8$: C, 61.98; H, 5.82; N, 5.78. Found: C, 62.25; H, 5.74; N, 5.89.

(7) Crascall, L. E.; Spencer, J. L. *Inorg. Synth.* **1990**, *28*, 126.

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Scheme 1

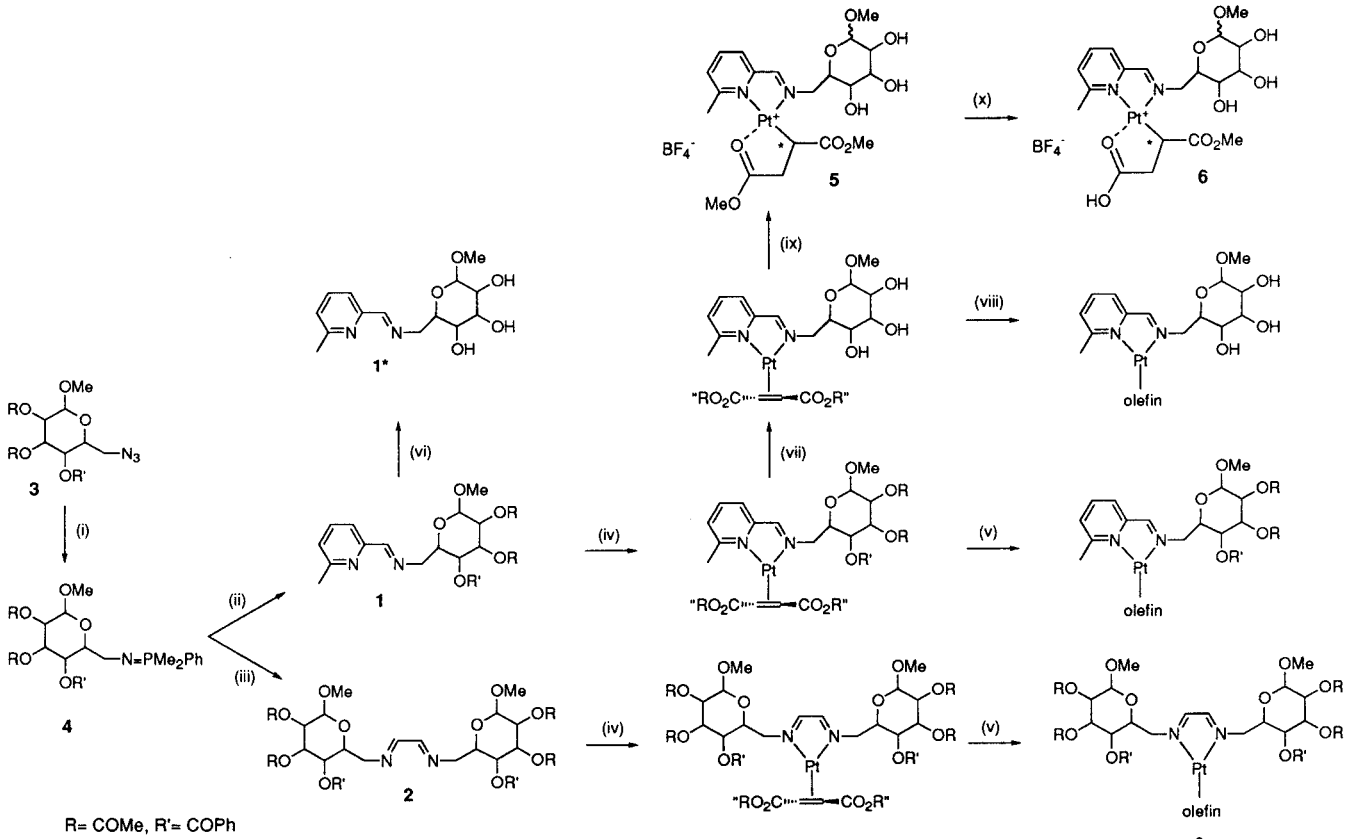

Table 1. [Pt(N,N-chelate)(η^2-olefin)] Complexes and Their Diastereomeric Equilibrium Composition[a]

[Pt(**1**)(η^2-(*E*)-$MeO_2CCH{=}CHCO_2Me$)][b]	1.3:1
[Pt(**1**)(η^2-(*E*)-NCCH=CHCN)][b]	1.2:1
[Pt(**1**)(η^2-$C_4H_2O_3$)][b]	1.3:1
[Pt(**2**)(η^2-(*E*)-$PhO_2CCH{=}CHCO_2Ph$)][b]	1:2.7
[Pt(**2**)(η^2-(*E*)-$MeO_2CCH{=}CHCO_2Me$)][b]	6:1
[Pt(**2**)(η^2-(*E*)-NCCH=CHCN)][b]	1:2.5
[Pt(**2**)(η^2-$C_4H_2O_3$)][b]	*c*
[Pt(**1***)(η^2-(*E*)-$MeO_2CCH{=}CHCO_2Me$)][d]	1.3:1
[Pt(**1***)(η^2-(*E*)-NCCH=CHCN)][d,e]	1.2:1
[Pt(**1***)(η^2-$C_4H_2O_3$)][d]	1:2.5

[a] At 298 K. The first figure refers to the first-formed isomer, quantitatively obtained through a second-order transformation. [b] In $CDCl_3$. [c] Formation of only one isomer is theoretically possible. [d] In D_2O. [e] A freshly dissolved sample already disclosed significant amounts of both diastereomers.

derivatives of fumarodinitrile ((*E*)-NCCH=CHCN) or maleic anhydride ($C_4H_2O_3$) were obtained by displacing the fumaric ester according to path v. The complexes were found to be readily soluble in chlorinated solvents but insoluble in water.

As expected, the hydrophilicity of the chelate was strongly enhanced by removing the alcoholic functions on the sugar residue. When **1** was treated in methanol containing a catalytic amount of sodium methoxide, the corresponding water-soluble ligand **1*** formed (vi). This ligand was always accompanied by another species, which made difficult the isolation of **1*** in pure form.[9]

For this reason, hydrolytic treatment was more conveniently performed on [Pt(**1**)(η^2-(*E*)-MeO_2C-$CH{=}CHCO_2Me$)], which selectively afforded the corresponding water-soluble complex [Pt(**1***)(η^2-(*E*)-MeO_2-$CCH{=}CHCO_2Me$)] in high yield (vii).[10] By using this compound as a precursor, water-soluble complexes of other olefins were obtained according to path viii.[11]

All the compounds were characterized by elemental analysis and NMR spectroscopy.[12] They are stable in solution for several hours, until the appearance of signals pertaining to the free olefin suggests the occurrence of some decomposition process. In no case were aldehyde signals observed, which indicates that the imine bond in the coordinated ligands is stable.

The number of possible isomers for each platinum complex is dictated by the symmetry of both ligands. More precisely, prochiral olefins (fumarodinitrile and

(8) Synthesis of [Pt(**1**)(η^2-(*E*)-$MeO_2CCH{=}CHCO_2Me$)]: to a stirred solution of the olefin (0.14 g, 1.0 mmol) in dry diethyl ether (10 mL) was added solid [Pt(η^2-norbornene)$_3$] (0.48 g, 1.0 mmol). The resulting solution was added to a suspension of the N,N-ligand (0.50 g, 1.0 mmol) in 3−4 mL of dry diethyl ether. After 24 h of stirring the orange-red crystals of the product were separated, washed with diethyl ether (3 × 4 mL), and dried under vacuum (yield >75%). Selected ^{1}H NMR resonances [in $CDCl_3$, $CHCl_3$ (δ 7.26) as internal standard, at 250 MHz, δ]: major isomer 9.03 ($^3J_{Pt-H}$ = 53 Hz, s, 1H, CH=N), 3.72 ($^2J_{Pt-H}$ = 90 Hz, s, 2H, HC=CH), 3.79, 3.57, and 3.35 (s, 9H, OMe), 2.92 (s, 3H, *Me*-py), 2.18 and 1.89 (s, 6H, $MeCO_2$); minor isomer 9.09 ($^3J_{Pt-H}$ = 55 Hz, s, 1H, CH=N), 3.68 (AB q, 2H, HC=CH), 3.55, 3.46, and 3.12 (s, 9H, OMe), 2.95 (s, 3H, *Me*-py), 2.16 and 1.88 (s, 6H, $MeCO_2$). Selected ^{13}C NMR resonances [in $CDCl_3$, $CDCl_3$ (δ 77) as internal standard, at 50.3 MHz, δ]: major isomer 167.3 (1C, CH=N), 25.1 ($^1J_{Pt-C}$ = 415 Hz, 1C, HC=CH), 24.3 ($^1J_{Pt-C}$ = 430 Hz, 1C, HC=CH); minor isomer 163.0 (1C, CH=N), 25.2 ($^1J_{Pt-C}$ = 411 Hz, 1C, HC=CH), 24.5 ($^1J_{Pt-C}$ = 414 Hz, 1C, HC=CH). Anal. Calcd for $C_{31}H_{36}N_2O_{12}Pt$: C, 45.20; H, 4.40; N, 3.40. Found: C, 45.18; H, 4.55; N, 3.26.

(9) The NMR spectrum of the crude product displayed a small amount of aldehyde, while preliminary attempts to purify **1*** resulted in extensive hydrolysis of the imine bond.

fumaric esters) can afford two diastereomers, depending on whether the alkene coordinates *re* or *si*. In all cases, the NMR spectra of freshly dissolved samples suggested that the complexes crystallized in pure diastereomeric form[13] due to second-order asymmetric transformation.[14] On standing in solution a slow epimerization process led to an equilibrium mixture within a few hours (see Table 1). According to the diastereomeric ratios at equilibrium, ligand **2** was more effective than **1** or **1*** in inducing stereoselective coordination of prochiral olefins. The equilibrium ratio was always higher than 2.5 in the presence of **2**, while in the case of **1** or **1*** the value dropped to ca. 1.3:1. The most pronounced case was [Pt(**2**)(η^2-(*E*)-$MeO_2CCH{=}CHCO_2Me$)], which consisted of diastereomers in a 6:1 ratio. This value is slightly higher than that recently measured for a series of *trans*-stilbene complexes of chiral diphosphines [Pt(P,P-chelate)(η^2-(*E*)-PhCH=CHPh)].[15]

Maleic anhydride can give rise to only one type **2** derivative, while diastereomers are theoretically possible for the complexes of **1** and **1***. The corresponding equilibrium ratios are reported in Table 1.

The ability of **1*** to induce a stereoselective reaction in water was preliminarily investigated. As it is known that olefin Pt(0) complexes undergo electrophilic attack by protic acids,[16] we added HBF_4 to the diastereomeric equilibrium mixture of [Pt(**1***)(η^2-(*E*)-$MeO_2CCH{=}CHCO_2Me$)] in D_2O (path ix). A transient product was observed in the early stages of the reaction. The presence of one methoxy resonance at δ 4.20 suggests formation of the cyclometalated product **5**,[17] similar to what is found in related insertion processes.[16] Subsequent disappearance of the signal at δ 4.20 and stoichiometric concomitant formation of methanol are compatible with the hydrolysis of one carboxymethyl group,[18] possibly activated by its coordination to Pt. After 24 h formation of **6** was quantitative (x).[19] According to the NMR spectra formation of the new stereogenic carbon (indicated with an asterisk) occurred with significant stereoselectivity (ee > 70%).[20]

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Supporting Information Available: Text and tables giving experimental details, NMR data, and elemental analyses of the complexes (7 pages). Ordering information is given on any current masthead page.

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(10) Synthesis of [Pt(**1***)(η^2-(*E*)-$MeO_2CCH{=}CHCO_2Me$)]: to a stirred suspension of [Pt(**1**)(η^2-(*E*)-$MeO_2CCH{=}CHCO_2Me$)] (0.50 g, 0.60 mmol) in 5 mL of dry methanol was added a catalytic amount of sodium methoxide in methanol. After 30 min formation of a solution was observed, followed by precipitation of the yellow product. After a further 16 h of stirring the complex was separated, washed with cold methanol (3 × 3 mL), and dried under vacuum (0.30 g, yield: 79%). Selected ^{1}H NMR resonances [in D_2O, DHO (δ 4.8) as internal standard, at 250 MHz, δ]: major isomer 9.40 ($^3J_{Pt-H}$ = 60 Hz, s, 1H, CH=N), 3.75, 3.69, and 3.47 (s, 9H, OMe), 2.91 (s, 3H, *Me*-py); minor isomer 9.35 ($^3J_{Pt-H}$ = 60 Hz, s, 1H, CH=N), 3.78, 3.71, and 3.28 (9H, s, OMe), 2.95 (s, 3H, *Me*-py). Selected ^{13}C NMR resonances [in $CDCl_3$, $CDCl_3$ (δ 77) as internal standard, at 50.3 MHz, δ]: major isomer 166.5 (1C, CH=N), 26.6 (1C, HC=CH), 23.4 ($^1J_{Pt-C}$ = 416 Hz, 1C, HC=CH); minor isomer 166.6 (1C, CH=N), 25.5 ($^1J_{Pt-C}$ = 405 Hz, 1C, HC=CH), 24.3 ($^1J_{Pt-C}$ = 414 Hz, 1C, HC=CH). Anal. Calcd for $C_{20}H_{28}N_2O_9Pt$: C, 37.80; H, 4.44; N, 4.41. Found: C, 37.93; H, 4.57; N, 4.27.

(11) Water-soluble platinum(0) complexes are rare. For some recent examples, see: (a) Darensbourg, D. J.; Decuir, T. J.; Stafford, N. W.; Robertson, J. B.; Draper, J. D.; Reibenspies, J. H.; Kathò, A.; Joò, F. *Inorg. Chem.* **1997**, *36*, 4218. (b) Ellis, J. W.; Harrison, K. N.; Hoye, P. A. T.; Orpen, A. G.; Pringle, P. G.; Smith, M. B. *Inorg. Chem.* **1992**, *31*, 3026.

(12) Elemental analyses and ^{1}H and ^{13}C NMR spectra for the new complexes are reported in Tables S1−3 of the Supporting Information.

(13) The only exception was represented by [Pt(**1***)(η^2-(*E*)-NCCH=CHCN)]. Actually, the NMR spectrum of a fresh solution of the complex already disclosed significant amounts of both diastereomers.

(14) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: London, 1962; p 49.

(15) Wicht, D. K.; Zhuravel, M. A.; Gregush, R. V.; Glueck, D. S.; Guzei, I. A.; Liable-Sands, L. M.; Rheingold, A. L. *Organometallics* **1998**, *17*, 1412.

(16) De Felice, V.; De Renzi, A.; Ruffo, F.; Tesauro, D. *Inorg. Chim. Acta* **1994**, *219*, 169.

(17) The magnitude (90 Hz) of the $^3J_{Pt-H}$ coupling constant of the imine proton in **5** points to the imine nitrogen atom being *trans* to oxygen. See: Albano, V. G.; Braga, D.; De Felice, V.; Panunzi, A.; Vitagliano, A. *Organometallics* **1987**, *6*, 517.

(18) This result was confirmed by performing the addition of HBF_4 to [Pt(**1***)((*E*)-$CD_3O_2CH{=}CHCO_2CD_3$)].

(19) Product **5** could be isolated by carrying out the reaction in dry toluene. Dissolution of this complex in D_2O resulted in hydrolysis of one carboxymethyl group and formation of **6** within 12 h.

(20) The reaction was accompanied by the occurrence of the equilibrium $C_1(\alpha) \rightleftarrows C_1(\beta)$, involving the anomeric carbon atom of the carbohydrate residue. The isomerization, which is in keeping with the presence of an acidic reagent, may represent a drawback for the use of **1*** or other carbohydrate-based ligands in processes promoted by metals, since the stereochemical stability of the ancillary ligands is an important requirement. Nevertheless, the enantiomeric excess observed in this preliminary test is encouraging. Furthermore, it should be noted that the equilibrium $C_1(\alpha) \rightleftarrows C_1(\beta)$ takes place only in acidic solutions, while in neutral or alkaline media the anomeric carbon atoms are known to be configurationally stable.