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olefins lying within the trigonal plane are characteristic of three-coordinate platinum(0) complexes.[1c,4c,6] Replacement of an axial electronegative chlorine atom with an electron-donating methyl group leads to increased π back bonding between the platinum metal and the coordinated olefins. It has been found that the olefin exchange and transmetallation reactions are sluggish in these five-coordinate complexes.

We present here the synthesis and spectral and structural characterization of the trisolefin platinum(II) trigonal-bipyramidal complexes. We find very good agreement between the various derivative structures determined in solution with that found for the parent compound in the solid state.

Experimental Section

General. ^{1}H NMR spectra were recorded at 300.154 MHz with a General Electric QE300 instrument (reference δ 7.27, $CHCl_3$). ^{13}C NMR spectra were recorded at 75.48 MHz with the same instrument (reference δ 77.0, $CDCl_3$ center peak). ^{195}Pt NMR spectra were recorded at 64.21 MHz with a Nicolet 300 widebore instrument (reference δ 0.0, aqueous K_2PtCl_6, $\Delta\nu_{1/2}$ = 34 Hz). On the Varian 500, ^{1}H NMR spectra were recorded at 499.84 MHz. All NMR spectra were determined in $CDCl_3$ or in C_6D_6 when specified (reference δ 7.24, C_6D_5H).

IR spectra were recorded on a Nicolet 5-DX FTIR spectrometer or on a Perkin Elmer 283 spectrometer with polystyrene calibration at 3027.1 and 1601.4 cm^{-1}. Complexes in solution were studied in $CDCl_3$ with KBr window solution cells. Solid complexes were studied as a Nujol mull between polyethylene windows in the 500–200-cm^{-1} region.

UV–visible spectra were obtained on a Hewlett-Packard 8451A diode array instrument using quartz cells with a path length of 0.1 cm.

Conductances were obtained with a YSI Scientific Model 35 conductance meter. This is a bridge circuit conductance meter used with the YSI 3403 dip cells, containing a platinized–iridium electrode with a cell body of Pyrex 7740.

Elemental analyses was performed by Desert Analytics, Tucson, AZ.

Reagent grade chemicals and solvents, including deuterated solvents, were purchased from Aldrich, Fischer, Union Carbide, Matheson, or Mallinckrodt. Sodium hydride, tetramethyltin, adamantane, methyltriphenyphosphonium bromide, and sodium hexachloroplatinate(IV) hexahydrate were all purchased from Aldrich Chemicals. Electrolytically reduced iron was purchased from Mallinckrodt. K_2PtCl_4 was a loan from Johnson Matthey Co.

Atom-Labeling Scheme. The carbon labeling is given in Figure 1. In particular all atoms associated with the monoolefins are primed. When the two apical directions of the trigonal bipyramid must be distinguished, we use the letters A and B which conform to the chlorine atom labels. The X and N notations on the hydrogen atoms refer to exo and endo orientations respectively.

Preparation of Compounds. 7-Methylenebicyclo[3.3.1]nonan-3-one. Adamantane (25 g) was brominated with liquid bromine in the presence of electrolytically reduced iron.[7] Adamantane was admitted to the reaction flask by way of a solid addition funnel. The apparatus was fitted with a cold finger which led to a water trip in order to dissolve vapors generated during the reaction. The reaction mixture was stirred for 5 h at room temperature. After being stirred, the mixture was added to 500 mL of ice water.[8] To the aqueous solution 450 mL of carbon tetrachloride was added. After separation the water layer was washed again with 300 mL of CCl_4, and the CCl_4 layers were combined. Saturated sodium bisulfite ($NaHSO_3$, 400 mL) was added in order to decompose any excess bromine. Solid sodium bisulfite was added to the mixture until the color changed from red to faint yellow. The CCl_4 layer was separated and further washed twice with 300 mL of 5% aqueous sodium bicarbonate ($NaHCO_3$). The CCl_4 layer was separated and the solvent was allowed to evaporate leaving the crude product 1,3-dibromoadamantane in 85% yield. 1,3-Dibromoadamantane (10 g) was added to 200 mL of a 1:1 mixture of dioxane and 1 M aqueous potassium hydroxide solution.[9] This solution was stirred at 140 °C for 14 h in a steel autoclave. The solution was filtered, and the filtrate was placed on a rotory evaporator at 50 °C under reduced pressure in order to remove the dioxane. The solid that precipitated out of solution was then filtered and dissolved in hot petroleum ether, which was then allowed to evaporate leaving 7-methylenebicyclo[3.3.1]nonan-3-one in 84% yield (overall 71%), mp 160 °C (lit. mp 160–164 °C).[9]

^{1}H NMR: δ 4.79 (2 H, singlet), 2.41–2.23 (10 H, multiplet), 1.94 (2 H, singlet): $\nu_{C=O}$ = 1700 cm^{-1} (lit. ^{1}H NMR: δ 4.77 (2 H), 2.38 (10 H), 1.94 (2 H); $\nu_{C=O}$ = 1720 cm^{-1}).[10]

3,7-Dimethylenebicyclo[3.3.1]nonane [DMBN]. A Wittig reaction was carried out on the ketone in order to obtain 3,7-dimethylenebicyclo-[3.3.1]nonane. The ylide used was formed from methylsulfinyl carbanion–dimethyl sulfoxide and methyltriphenyphosphonium bromide.[11] The ylide (.035 mol) reagent 60% in excess was heated with the ketone (0.02 mol) for 17 h at 60 °C. The solution was poured into 40 mL of water. The aqueous phase was extracted with 100-, 75-, and 50-mL portions of *n*-pentane. The combined pentane layers were washed with 100 mL of a 1:1 water–dimethyl sulfoxide solution and then with 200 mL of a 50% saturated sodium chloride solution. The pentane layer was evaporated yielding the crude product. Purification of 3,7-dimethylenebicyclo-[3.3.1]nonane was done by room temperature sublimation in a closed system under reduced pressure giving an isolated yield of 48%, mp 77–79 °C (lit. mp 75 °C).[12]

^{1}H NMR: δ 4.56 (4 H, $=CH_2$), 2.35 (8 H, $-CH_2-$, allylic), 2.05 (2 H, –CH–), 1.72 (2 H, $-CH_2$, bridge) [lit. ^{1}H NMR: δ 4.57 (4 H, $=CH_2$), 2.38 (8 H, $-CH_2-$, allylic), 2.04 (2 H, –CH–), 1.73 (2 H, $-CH_2$, bridge)].[13]

^{13}C NMR: δ 145.80 (C3, C7), 110.00 (C10, C11), 40.61 (C2, C4, C6, C8), 33.41 (C9), 29.08 (C1, C5) [lit. ^{13}C NMR: δ 145.2 (C3, C7), 110.4 (C10, C11), 40.8 (C2, C4, C6, C8), 33.7 (C9), 29.4 (C1, C5)].[14]

IR (cm^{-1}): 3072 (m), 2979 (m), 2921 (s), 2825 (m), 1648 (m), 1472 (m), 1433 (m).

***trans*-Dichloro(η^2-ethylene)[(3,10,7,11-η^4)-3,7-dimethylenebicyclo-[3.3.1]nonane]platinum(II) [(DMBN)(C_2H_4)$PtCl_2$, 1].** Di-μ-chloro-dichlorobis(η^2-ethylene)diplatinum(II)[15] (Zeise's dimer) (141.1 mg, 0.24 mmol) and 3,7-dimethylenebicyclo[3.3.1]nonane (71.04 mg, 0.48 mmol) were mixed together in 4.5 mL of $CDCl_3$ in a 25-mL round-bottom flask. A yellow solution was obtained upon mixing. The solution volume was then reduced to 1 mL by evaporation under vacuum. After addition of 2 mL of hexane the flask was sealed and stored at −24 °C for 2 days, over which time a yellow precipitate formed. The yellow solid was filtered at 4 °C and stored in the dark at room temperature. After 7 days storage at room temperature decomposition of the product was detected. Anal. Calcd for $C_{13}H_{20}PtCl_2$: C, 35.30; H, 4.56. Found: C, 35.53; H, 4.41.

^{1}H NMR (T = 23 °C): δ 4.57 (H10A, H10B, H11A, H11B, J_{Pt-H} = 56.7 Hz), 4.39 (H1A′, H1B′, H2A′, H2B′, J_{Pt-H} = 58.6 Hz), 2.46 (H1, H5), 2.09 (H2N, H2X, H4N, H4X, H6N, H6X, H8N, H8X), 1.92 (H9L, H9R). All vicinal DMBN aliphatic proton–proton coupling constants are 3 Hz. No proton gem couplings were detected.

^{1}H NMR (T = 055 °C): δ 4.55 (H10A, H10B, H11A, H11B, J_{Pt-H} = 54.4 Hz), 4.38 (H1A′, H1B′, H2A′, H2B′, J_{Pt-H} = 56.3 Hz), 2.48 (H1, H5). The assignments of the following two resonances could be reversed: δ 2.08 (H2X, H4X, H6X, H8X) and 1.98 (H2N, H4N, H6N, H8N), 1.92 (H9L, H9R). DMBN coupling constants: $J_{H2N-H2X}$, $J_{H4N-H4X}$, $J_{H6N-H6X}$, $J_{H8N-H8X}$ = 15.1 Hz.

^{1}H NMR (in C_6D_6, T = 23 °C): δ 4.51 (H10A, H10B, H11A, H11B, J_{Pt-H} = 57.1 Hz), 4.44 (H1A′, H1B′, H2A′, H2B′, J_{Pt-H} = 59.1 Hz). As above these two resonances could have their assignments reversed: δ 2.16 (H2X, H4X, H6X, H8X) and 1.74 (H2N, H4N, H6N, H8N), 2.08 (H1, H5), 1.48 (H9L, H9R). DMBN coupling constants: $J_{H2N-H2X}$, $J_{H4N-H4X}$, $J_{H6N-H6X}$, $J_{H8N-H8X}$ = 15.1 Hz.

^{13}C NMR: δ 122.42 (C3, C7, J_{Pt-C} = 22.0 Hz), 67.29 (C10, C11, J_{Pt-C} = 90.3 Hz), 55.89 (C1′, C2′, J_{Pt-C} = 159.6 Hz), 35.00 (C1, C5, 34.84 (C2, C4, C6, C8), 33.87 (C9).

^{195}Pt NMR: δ (−)2797.58.

IR (cm^{-1}): 2968 (m), 2918 (s), 2877 (m), 2853 (m), 2823 (m), 1514 (m), 1455 (m), 1429 (s), 1418 (m), 330 (m).

(6) (a) Rosch, N.; Hoffmann, R. *Inorg. Chem.* **1974**, *13*, *No. 11*, 2656–2666. (b) Green, M.; Howard, J. A. K.; Spencer, J. L.; Stone, F. G. A. *J. Chem. Soc., Dalton* **1977**, 271–277. (c) Harrison, N. C.; Murray, M.; Spencer, J. L.; Stone, F. G. A. *J. Chem. Soc. Dalton* **1978**, 1337. (d) Chicote, M. T.; Green, M.; Spencer, J. L.; Stone, F. G. A.; Vincente, J. *J. Chem. Soc., Dalton* **1979**, 536–541.

(7) Likhotvorik, I. R.; Dovgan, N. L.; Danilenko, G. I. *Zh. Org. Khim.* **1977**, *13*, *No. 4*, 897.

(8) Talaty, E. R.; Cancienne, A. E.; Dupuy, A. E. *J. Chem. Soc. C* **1968**, 1902–1903.

(9) (a) Geigy, J. R. British Patent No. 1,095,780. (b) Stetter, H.; Tacke, P. *Chem. Ber.* **1963**, *96*, 694–698.

(10) Gagneux, R.; Meier, R. *Tetrahedron Lett.* **1969**, *17*, 1365–1368.

(11) Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128–1129.

(12) Stetter, H.; Gartner, J.; Tacke, P. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 153–154.

(13) Krasutskii, P. A.; Yurchenko, A. G.; Jones, M.; Kornilov, M. Y.; Degtyarev, L. S.; Zamkovoi, V. I. *Teor. Eksp. Khim.* **1982**, *18*, *No. 2*, 189–193.

(14) Sendra, Y.; Ishiyama, J.; Imaizumi, S. *J. Chem. Soc., Perkins II* **1981**, *1*, 90–93.

(15) Busse, P. J.; Greene, B.; Orchin, M. *Inorg. Synth.* **1980**, *20*, 181–185.

UV (in $CDCl_3$): λ = 232 nm (ϵ = 16 833 mol/cm); λ = 346 nm (ϵ = 7112 mol/cm).

UV (in CH_2Cl_2): λ = 230 nm (ϵ = 35 500 mol/cm); λ = 348 nm (ϵ = 7329 mol/cm).

The compound is nonconducting in $CDCl_3$.

Growth of Single Crystals of 1. Zeise's dimer (141.1 mg, 0.24 mmol) was reacted with DMBN (71.04 mg, 0.48 mmol) in 4.5 mL of $CDCl_3$. The reaction mixture was stirred for 2 min and the solvent concentrated to 0.5 mL under reduced pressure. A 10-fold amount of hexane (5 mL) was added and the solution was concentrated under vacuum until solid started to form. The solution was then stored at −24 °C overnight. This led to large yellow crystals. One was selected for X-ray diffraction and was cut with a razor blade to give a crystal fragment with better dimensions (*a*, *b*, *c* = 0.38, 0.15, 0.18 mm).

***trans*-Chloromethyl(η^2-ethylene)[(3,10,7,11-η^4)-3,7-dimethylenebicyclo[3.3.1]nonane]platinum(II) [(DMBN)(C_2H_4)(CH_3PtCl), 2].** Tetramethyltin (9.96 μL, 0.072 mmol) was added in 50% excess to Zeise's dimer (14.1 mg, 0.024 mmol) in 0.4 mL of $CDCl_3$, forming di-μ-chloro-dimethyl(η^2-ethylene)diplatinum(II).[16] ^{1}H NMR: δ 3.90 (4 H, $=CH_2$, ethylene), 0.6 (6 H, methyl). After 2 min of mixing 3,7-dimethylenebicyclo[3.3.1]nonane (7.1 mg, 0.048 mmol) was added to the reaction mixture. The reaction was allowed to proceed an additional 2 min before removing the solvent under reduced pressure. The product was redissolved in $CDCl_3$ and lyophilized three more times to remove residual traces of organotins.

^{1}H NMR (olefinic region) methyl face: δ 8.54 (H10A, H11A, J_{Pt-H} = 55.5 Hz), 3.18–3.16 (H1A′, H2A′, J_{Pt-H} = 55.6 Hz); chlorine face: δ 4.19 (H10B, H11B, J_{Pt-H} = 58.4 Hz), 4.04–4.02 (H1B′, H2B′, J_{Pt-H} = 63.4 Hz)

Olefinic hydrogen ethylene couplings (Hz): $J_{H1A'-H2B'}$, $J_{H1B'-H2A'}$ = 12.7; $J_{H1A'-H2A'}$, $J_{H1B'-H2B'}$ = 9.7; $J_{H1A'-H1B'}$, $J_{H2A'-H2B'}$ = 0.0.

Olefinic hydrogen DMBN couplings (Hz): $J_{H10A-H10B}$, $J_{H11A-H11B}$ = 1.1 Hz.

^{1}H NMR (aliphatic region) methyl face: δ 2.15–2.11 (H2X, H8X), 1.38–1.35 (H2N, H8N), 2.49 (H1); chlorine face: δ 2.42–2.39 (H4N, H6N), 2.31–2.29 (H4X, H6X), 2.44 (H5). Bridge hydrogens δ 1.93 (H9L, H9R). Methyl hydrogens δ −0.61 (3 H, Pt−CH_3, J_{Pt-H} = 61.6 Hz).

Aliphatic hydrogen couplings (Hz): $J_{H2N-H2X}$, $J_{H8N,H8X}$ = 15.1; $J_{H4N-H4X}$, $J_{H6N-H6X}$ = 14.9; J_{H1-H2X}, J_{H1-H8X} = 3.5; J_{H1-H2N}, J_{H1-H8N} = 3.5; J_{H5-H4X}, J_{H5-H6X} = 3.6; J_{H5-H4N}, J_{H5-H6N} = 3.6; H9L, H9R shows a progression of couplings all equal to 1 Hz.

^{13}C NMR: δ 113.08 (C3, C7, J_{Pt-C} = 26.0 Hz), 61.19 (C10, C11, J_{Pt-C} = 108.8 Hz), 52.17 (C1′, C2′, J_{Pt-C} = 178.2 Hz), 36.15 (C5), 35.65 (C4, C6), 35.25 (C9), 34.60 (C1), 34.55 (C2, C8), −1.28 (C, Pt−CH_3, J_{Pt-C} = 616.8 Hz).

IR (cm^{-1}): 2966 (m), 2917 (s), 2856 (m), 2826 (m), 1602 (m), 1465 (m), 1432 (m).

UV (in $CDCl_3$): λ = 240 nm (ϵ = 5137 mol/cm).

UV (in CH_2Cl_2): λ = 222 nm (ϵ = 8356 mol/cm).

***trans*-Dichloro(η^2-olefin)[(3,10,7,11-η^4)-3,7-dimethylenebicyclo-[3.3.1]nonane]platinum(II) [(DMBN)(olefin)$PtCl_2$, 4a–c: Olefin = (a) Propylene, (b) *cis*-2-Butene, (c) *trans*-2-Butene].** The respective olefins were bubbled slowly through a 0.4-mL $CDCl_3$ solution containing Zeise's dimer (7.1 mg, 0.012 mmol) for 2 min and then the solution was flushed with a slow nitrogen flow for 2 min. The above bubbling and flushing process was repeated once again. The corresponding di-μ-chloro-dichlorobis(η^2-olefin)diplatinum(II) complexes **3a–c** were isolated by removing the solvent and excess olefin gases under reduced pressure.

^{1}H NMR (**3a**): δ 5.67 (H2B′), 4.83 (H1B′), 4.62 (H1A′), 1.71 (3H3A′). Coupling constants (Hz): $J_{H1A'-H2B'}$ = 13.5, $J_{H1B'-H2B'}$ = 7.45, $J_{H3A'-H2B'}$ = 6.3.

^{1}H NMR (**3b**): δ 5.71–5.48 (H1B′, H2B′), 1.68–1.43 (3H3A′, 3H4A′).

^{1}H NMR (**3c**): δ 5.56–5.06 (H1A′, H2B′), 1.86–1.34 (3H3B′, 3H4A′).

The dimers **3a–c** were redissolved into 0.4 mL of $CDCl_3$ and 3,7-dimethylenebicyclo[3.3.1]nonane (3.6 mg, .024 mmol) was added to form the corresponding five-coordinate complexes **4a–c**. The following assignments are based on placing the first olefin substituent (e.g. the methyl group, C3′, of propylene) in the quadrant adjacent to H11A of DMBN. The second substituent, C4′, is then across from H10A or H10B depending on whether the monoolefin has cis or trans geometry.

[(DMBN)(propylene)$PtCl_2$] (4a). ^{1}H NMR (T = 23 °C): δ 5.34–4.91 (1 H, =CH, propylene), 4.85–4.03 (6 H, $=CH_2$, DMBN, propylene), 2.43 (2 H, −CH−, DMBN), 2.23–1.97 (8 H, $-CH_2-$, allylic, DMBN), 1.91 (2 H, $-CH_2-$, bridge, DMBN), 1.63–1.73 (3 H, $-CH_3$, propylene).

^{1}H NMR (T = −60 °C): propylene, δ 5.08 (H2B′), 4.48 (H1B′), 4.25 (H1A′), 1.71 (3H3A′); DMBN, δ 4.63 (H10B), 4.58 (H10A), 4.46 (H11B), 4.16 (H11A), 2.46 (H1), 2.44 (H5), 2.04 (H2N, H2X, H8N, H8X), 2.01 (H4N, H4X, H6N, H6X), 1.88 (H9L, H9R).

Olefinic hydrogen propylene couplings (Hz): $J_{H1A'-H2B'}$ = 13.5, $J_{H1B'-H2B'}$ = 7.5, $J_{H3A'-H2B'}$ = 6.4.

^{1}H NMR (in C_6D_6, T = 23 °C): δ 5.33–5.16 (1 H, =CH, propylene), 4.63–4.18 (6 H, $=CH_2$, DMBN, propylene), 2.31–1.63 (8 H, $-CH_2-$ allylic, DMBN, 3 H, $-CH_3$ propylene), 2.08 (2 H, −CH−, DMBN), 1.50 (2 H, $-CH_2-$, bridge, DMBN).

IR (cm^{-1}): 2969 (m), 2917 (s), 2876 (m), 2854 (m), 1511 (m), 1456 (m), 1429 (s).

[(DMBN)(*cis*-2-butene)$PtCl_2$] (4b). ^{1}H NMR (T = 23 °C): δ 5.57–5.10 (2 H, =CH—, butene), 4.70–4.24 (4 H, $=CH_2$, DMBN), 2.48–2.31 (2 H, −CH−, DMBN), 2.31–1.93 (8 H, $-CH_2-$, allylic, DMBN), 1.91 (2 H, $-CH_2-$, bridge, DMBN), 1.60 (6 H, $-CH_3$, butene).

^{1}H NMR (T = −60 °C): *cis*-2-butene, δ 6.19 (H1B′, H2B′, J_{Pt-H} = 64.1 Hz), 1.61 (3H3A′, 3H4A′); DMBN, δ 4.50 (H10B, H11B, J_{Pt-H} = 51.9 Hz), 4.28 (H10A, H11A, J_{Pt-H} = 51.9 Hz), 2.45 (H1), 2.39 (H5), 2.10 (H2X, H8X), 2.02 (H4X, H4N, H6X, H6N, 1.97 (H2N, H8N), 1.87 (H9L, H9R).

Hydrogen couplings (Hz): $J_{H4A'-H1B'}$ = 4.3, $J_{H3A'-H2B'}$ = 4.3, $J_{H2N-H2X}$ = 15.2, $J_{H8N-H8X}$ = 15.2.

IR (cm^{-1}): 2970 (m), 2914 (s), 2877 (s), 2856 (m), 2092 (m), 1511 (m), 1455 (m), 1429 (s).

[(DMBN)(*trans*-2-butene)$PtCl_2$] (4c). ^{1}H NMR (T = 23 °C): δ 5.25–4.92 (2 H, =CH, butene), 4.74–4.26 (4 H, $=CH_2$, DMBN), 2.48–2.31 (2 H, −CH−, DMBN), 2.31–1.93 (8 H, $-CH_2-$, allylic, DMBN), 1.91 (2 H, $-CH_2-$, bridge, DMBN), 1.69 (6 H, $-CH_3$, butene).

^{1}H NMR (T = −60 °C): *trans*-2-butene, δ 4.89 (H1A′, H2B′, J_{Pt-H} = 61.3 Hz), 1.70 (3H3A′, 3H4B′); DMBN, δ 4.67 (H10A, H11B, J_{Pt-H} = 53.7 Hz), 4.14 (H10B, H11A, J_{Pt-H} = 53.7 Hz), 2.42 (H1, H5), 2.13 (H4X, H8X), 2.01 (H2N, H2X, H6N, H6X), 1.99 (H4N, H8N), 1.87 (H9L, H9R).

Hydrogen couplings (Hz): $J_{H3A'-H2B'}$ = 4.1, $J_{H4B'-H1A'}$ = 4.1, $J_{H4N-H4X}$ = 14.9, $J_{H8N-H8X}$ = 14.9.

IR (cm^{-1}): 2966 (m), 2918 (s), 2879 (s), 2855 (m), 1515 (m), 1441 (m), 1429 (s).

***(trans*-Dichloro)(η^2-styrene)[(3,10,7,11-η^4-)-3,7-dimethylenebicyclo-[3.3.1]nonane]platinum(II) [(DMBN)(styrene)$PtCl_2$, 5].** DMBN (7.1 mg, 0.048 mmol) was added to a solution of 0.5 mL of $CDCl_3$ containing $[Pt(\mu\text{-Cl})Cl(PhCH{=}CH_2)]_2$[17] (17.8 mg, 0.024 mmol). ^{1}H NMR [Pt-(μ-Cl)Cl($PhCH{=}CH_2$)]$_2$, (T = 23 °C): δ 7.56 (2 H, phenyl), 7.50 (1 H, phenyl), 7.38 (2 H, phenyl), 6.54 (H2B′), 5.10 (H1A′, 4.77 (H1B′). Upon addition an orange solution was obtained.

^{1}H NMR (T = −60 °C): styrene, δ 7.60 (2 H, phenyl), 7.37 (2 H, phenyl), 7.35 (1 H, phenyl), 6.20 (H2B′, J_{Pt-H} = 65.6 Hz), 4.95 (H1A′), 4.62 (H1B′); DMBN, δ 4.77 (H10B), 4.73 (10A), 4.52 (H11B), 3.57 (H11A, J_{Pt-H} = 47.7 Hz), 2.44 (H5), 2.41 (H1), 2.07 (H2N, H2X, H4N, H4X, H6N, H6X), 1.87 (H8N, H8X, H9L, H9R).

Hydrogen couplings (Hz): $J_{H1B'-H2B'}$ = 8.6, $J_{H1A'-H2B'}$ = 13.0.

Crystallography. The crystal fragment (vide supra and Table I) was mounted on a glass fiber and ceramic pin and cooled to −79 °C in a N_2 stream (crystals become putty like and nondiffracting in ca. 2 h at room temperature) before crystal orientation and intensity data collection on an Enraf-Nonius CAD4 diffractometer. The space group $P2_1/c$ determined earlier by precession photographs taken in a 4 °C cold room was confirmed, and the cell constants were refined using 16 carefully centered reflections (13° < 2θ <46°). Data reduction, structure solution, and refinement were done with the SDP-VAX[18] suite of programs. The structure was solved by interpretation of a Patterson map and refined by full-matrix least squares where the function minimized was $\sum w(|F_o| - |F_c|)^2$ and the weight $w = 4F_o^2/[\sigma(I^2)]^2$. An empirical absorption correction to the intensities was based on a PSI scan of the 400 reflection followed by a DIFABS[18] correction for Bragg angle dependence. All non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were assigned temperature factors 20% larger than the bearing atom. Only the olefinic hydrogens were refined.

NMR Techniques. The assignments for the ^{1}H NMR olefinic resonances of complex **1** were resolved by using the spin saturation transfer technique. When free ethylene is added to a solution of complex **1**, ethylene exchange is observed to be slow on the ^{1}H NMR time scale,

(16) Scott, J. D.; Puddephatt, R. J. *J. Chem. Soc., Chem. Commun.* **1984**, 193–195.

(17) Albinati, A.; Caseri, W. R.; Pregosin, P. S. *Organometallics* **1987**, *6*, 788–793.

(18) LAOCN3 by A. A. Bothner-By and S. M. Castellano was adapted to the IBM-PC by R.M.W. See: DeTar, D. F., Ed. *Computer Programs for Chemistry*; W. A. Benjamin: New York, 1968; Vol. 1, Chapter 3.

Table I. Summary of Crystal Data for *trans*-Dichloro(η^2-ethylene)[(3,10,7,11-η^4)-3,7-dimethylenebicyclo-[3.3.1]nonane]platinum(II)

formula	$C_{13}H_{20}PtCl_2$
M, D	442.3
space group	$P2_1/c$, No. 14
a, Å	7.629 (1)
b, Å	12.431 (1)
c, Å	14.714 (2)
β, Å	100.87 (1)
V, Å^3	1370.6 (3)
T, °C	−79
z	4
d_{calc}, g/cm^3	2.146
cryst size (mm × mm × mm)	0.38, 0.15, 0.18
μ, cm^{-1}	107.3
radiation (graphite monochromated)	Mo Kα (λ = 0.7107 Å)
scan type	ω–2θ
scan width (ΔW), deg	1.00 + 0.35 tan θ
max scan time, s	120 $\theta < 20°$
	180 $20° < \theta < 25°$
	360 $25° < \theta < 30°$
data collection range	$1 < \theta < 30°$
no. of unique data	3990
no. of unique data $I > 3\sigma(I)$	3126
no. of variables of refined	169
R,[a] %	2.6
R_w,[b] %	3.8
esd[c]	1.3
largest parameter shift	0.05
largest residual electron density,[d] e/Å^3	0.95

[a] $R = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $R_w = \sum w(|F_o| - |F_c|)^2$, the weight w is $4F_o^2/[\sigma(I^2)]^2$, and $\sigma(I) = [P + 4B + (0.0451)^2]^{1/2}$. P is the number of counts observed during the scan, and B is the sum of background counts. [c] From final refinement. [d] From final difference fourier; this and the next 10 peaks were all within 1 Å of the Pt.

Thus the free ethylene is found at 5.42 ppm and none of the olefinic resonances associated with the complex are shifted or line broadened. Upon irradiation of the free ethylene at 5.42 ppm only the coordinated olefin resonance at 4.39 ppm decreases dramatically in intensity. A similar study was performed in the presence of excess Zeise's dimer. Once again the resonances associated with the coordinated olefinic protons are neither broadened nor shifted. Irradiation of the signal associated with Zeise's dimer again only decreases the intensity of resonance at 4.39 ppm. The study with excess free ethylene was repeated again also in the presence of excess ligand and identical results were obtained.

Assignments for the ^{13}C NMR olefinic carbons of complex **1** were made using resonance suppression via selective polarization transfer.[19] It was found that the coordinated ethylene ^1H NMR resonance at 4.39 ppm is associated with the ^{13}C NMR resonance at 55.89 ppm, and the ^1H NMR coordinated ligand resonance at 4.57 ppm is associated with the ^{13}C NMR resonance at 67.29 ppm.

The coupling constants of the quaternary carbons in compounds **1** and **2** were revealed by resolution enhancement of the F.I.D. by double exponential multiplication using the NICOLET/QE300 data processing software with DM = 7.

Only one ^{195}Pt NMR resonance was found in the chemical shift range +300 to −5000 ppm. A singlet at −2797 ppm was observed with a line width at 45 Hz when using broad-band proton decoupling. Turning the decoupler off indicates a 58-Hz coupling of the platinum to eight equivalent protons.

A variety of ^1H NMR techniques were employed in order to assign the proton resonances of complex **2**. The aliphatic proton resonances were assigned by performing selective proton decoupling experiments. This allowed for the assignments of all the allylic geminal protons and the bridging and bridgehead proton resonances. Assignment of olefinic resonances was done by spin saturation transfer as with complex **1**. Thus the multiplet patterns centered at 3.17 and 4.03 ppm were assigned to coordinated ethylene. The coupling constants of the coordinated ethylene resonances were determined by least-squares fitting of 8 experimentally determined resonance frequencies measured at 500 MHz with LAOCN3.[20] To distinguish which protons of the ligand and ethylene are directed toward the methyl group versus the chlorine atom, we used the Nuclear Overhauser Effect (NOE) technique. The axial methyl group was irradiated to give the NOE difference spectra of Figure 2. In the absence of excess ethylene, all endo allylic proton as well as olefinic proton resonances were NOE enhanced. This indicates fluxionality in the system. Exogenous ethylene quenches this fluxionality thus allowing facial assignment of the proton resonances. The following NOE enhancements were observed (%): DMBN allylic resonance at 1.38 ppm = 3.5, DMBN olefinic resonance at 3.54 ppm = 2.2, and ethylene resonance at 3.17 ppm = 3.7.

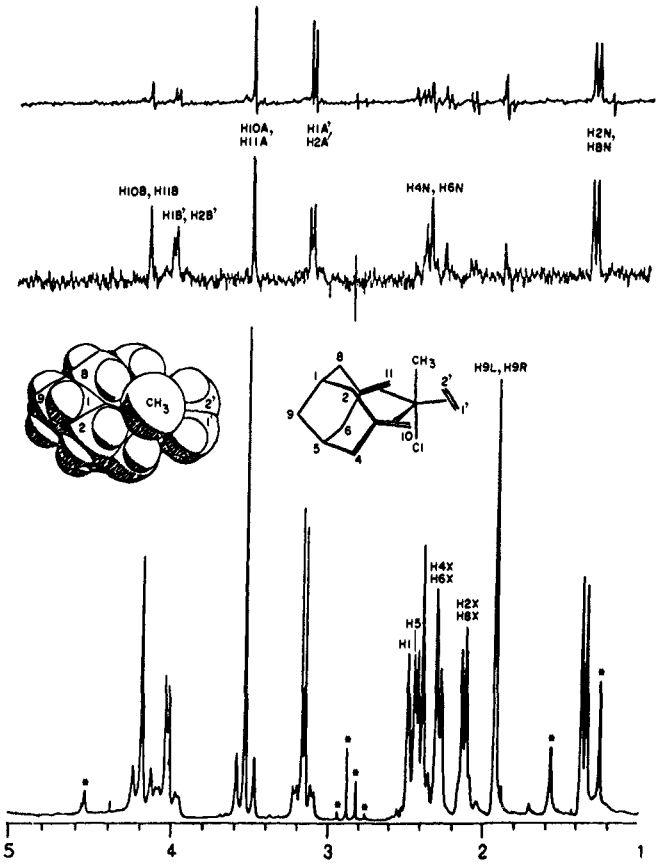
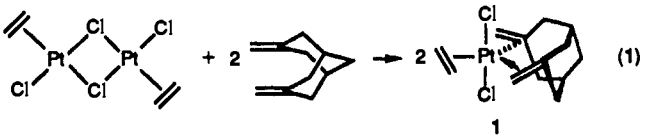


Figure 2. (A, bottom) ^1H NMR spectrum (500 MHz) of **1**. The methyl resonance (−0.65 ppm) has been omitted; peaks indicated with an asterisk are impurities. (B, middle) NOE difference spectrum resulting from irradiation of the axial methyl ligand. (C, top) NOE difference spectrum as in B, but with 10% excess ethylene added to the NMR sample.

For compounds **4a–c** and **5** all ^1H NMR spectra were determined at low temperature to suppress monoolefin dissociation. The monoolefin resonances were assigned by selective proton decoupling and by relating the observed coupling constants to those of the corresponding free olefin. The olefinic resonances of DMBN in each of these were assigned by observation of van der Waals shifts and coupling constants, and/or NOE difference spectroscopy. For example, the propylene derivative gave the following enhancements (%): proton gem to the methyl group of propylene 17.35, proton cis to the methyl group of propylene 4.05, and the olefinic proton of DMBN closest to this methyl group 4.02.

Results and Discussion

A. Preparation of Compounds. The formation of compound **1** was accomplished as shown in eq 1, where the bridging chloride is a good leaving group. DMBN however does not react with



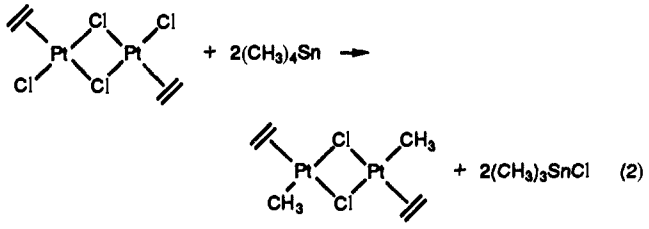
(1)

1

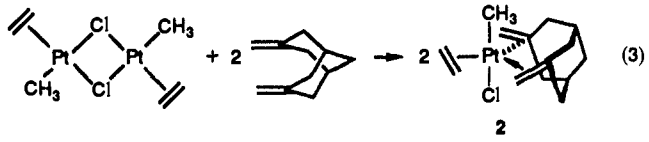
Zeise's anion in analogy to the formation of the five-coordinate complexes with diimines and diamines.[5a]

Compound **2** was synthesized from the methyl analogue of Zeise's dimer formed by reaction of Zeise's dimer with a 50% excess of the transmetallating reagent tetramethyltin as in eq 2. After removing the excess tin reagent by evaporation under

(19) Davis, D. G.; Live, D. H.; Agosta, W. C.; Cowburn, D. *J. Magn. Reson.* **1983**, *53*, 350–354.
(20) Enraf-Nonius, Bohemia, NY.



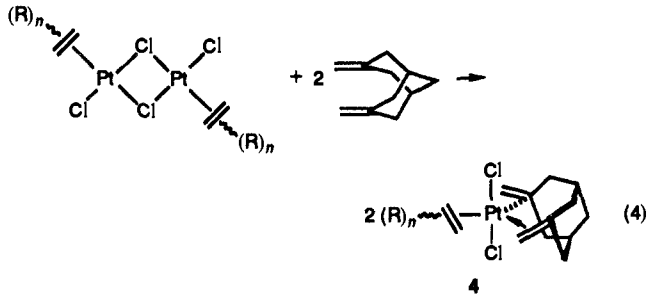
vacuum, DMBN was added to give compound **2** (eq 3).



2

Compound **2** can, with great difficulty, be synthesized by direct reaction of tetramethyltin with compound **1**. This reaction is however extremely slow, taking many hours during which copious amounts of side products are produced. It is believed that transmetallation of the five-coordinate structure is much slower then transmetallation of the four-coordinate Zeise's dimer due to the steric crowding that is encountered in the proposed four-centered transition state.[21] Both preparations give the same yellow-orange color and the isolated product is stable at $T = -24$ °C. At room temperature over the course of days it decomposes or rearranges.

In preparing the monoolefin complexes **4a–c** (eq 4) we utilized



4

R = CH_3 (**a**), *cis*-1,2-CH_3 (**b**), *trans*-1,2-CH_3 (**c**)

the fact that olefin exchange on Zeise's dimer is facile, whereas olefin exchange with the five-coordinate complexes is sluggish. In general it was found that the processes of transmetallation and olefin exchange are much faster and cleaner with the four-coordinate platinum complexes vs. the five-coordinate ones. Thus Zeise's dimer analogues are convenient precursors to all five-coordinate complexes reported here.

B. Structural and Spectroscopic Considerations. 1. Crystal Structure. The crystal structure of the parent compound [(DMBN)(C_2H_4)$PtCl_2$, **1**] has been determined (Figure 1). The molecular symmetry is C_{2v} with all three olefins coordinated at the equatorial positions of a trigonal bipyramid and the two chlorine atoms occupying the axial sites. As illustrated in Figure 3, the diene (DMBN) and ethylene are both bisected by the 2-fold axis and one of the mirror planes. The three olefins are found to lie in the mirror defined by the trigonal plane; there is less than one standard deviation between the trigonal plane and any olefinic carbon atom. The angle formed by DMBN double bond centroids with Pt as the apex is 103.8°, and it is very similar to the "bite angle" of DMBN coordinated to Ag^+ which is 109.0°.[22] This is however accomplished by distorting the quaternary carbons C3 and C7 from planarity by about 15.4 (9)° which is 28% of the way to tetrahedral geometry. Otherwise the DMBN ligand undergoes little distortion upon coordination, and in view of the fact

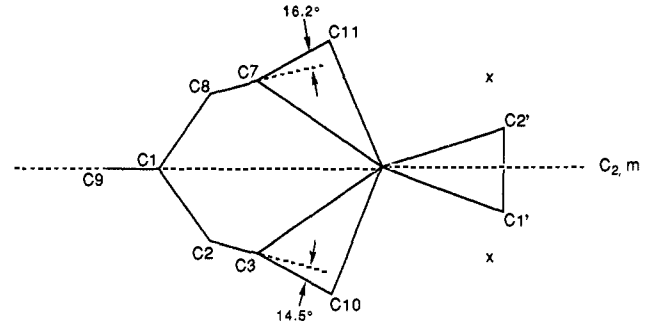


Figure 3. Projection of **1** onto the trigonal mirror plane, showing the nonplanarity of C3 and C7 and the skewness of the DMBN ligand coordination to the metal. The X's mark the positions computed for chlorine in the hypothetical minimum free energy square planar complex (see text). The chlorine atoms have been omitted entirely and the labels for Pt, C4, C5, and C6 have been omitted.

that out-of-plane distortions of planar systems are rather facile, there is presumably little enthalpic penalty for coordination. The chlorine atoms are bent back away from the complexed diene DMBN toward the coordinated ethylene, but still remain in the mirror, so that the angle between the Cl–Pt bonds is 173.13 (5)°. This distortion arises from short chlorine to DMBN contacts,[23] the most significant being with hydrogens H2N, H8N, H4N, and H6N all equal to 2.64 Å. The other significant contacts are with the olefinic H's. These are 2.80 Å to the DMBN methylene protons (H10A, H10B, H11A, H11B) and balancing the distortion are the ethylene protons (H1A′, H1B′, H2A′, H2B′) at 2.68 Å. These close contacts are most apparent in complex **2** in which their resonances are Nuclear Overhauser Enhanced when the axial methyl group is irradiated (Figure 2), with just those protons mentioned above gaining intensity. The coordination of the platinum atom to the olefins of DMBN is very unsymmetrical. The platinum distance to the methylene carbons to DMBN Pt–C10, Pt–C11 is 2.254 (5) Å vs. 2.475 (7) Å to the quaternary carbons Pt–C3; Pt–C7. The interaction of the platinum atom with ethylene carbons Pt–C1′, Pt–C2′ is considerably stronger and more symmetric, 2.154 (7) Å. The varying bond distances of the platinum center to the olefinic carbons in the crystal structure are readily apparent in solution. Shorter platinum–carbon bond distances are reflected in larger upfield carbon coordination chemical shifts ($\Delta\delta$), and larger platinum–carbon coupling constants. Thus the trend in progressing from long to short bond lengths is $\Delta\delta$ (ppm)/J (Hz); 23/22, 43/90, 67/159,

2. Spectroscopic Data. The solution infrared spectra of compounds **1**, **2**, **4a–c**, and DMBN were determined in $CDCl_3$. The uncomplexed ligand exhibits two prominent medium peaks at 1647 and 3072 cm^{-1} which are characteristic of the C=CH_2 functional group.[24] In all of the five-coordinate compounds the 2072-cm^{-1} peak is absent and the 1647-cm^{-1} peak is shifted to lower energy: to 1602 cm^{-1} for compound **2** and varying between 1515 and 1511 cm^{-1} for compounds **1** and **4a–c**. The lowered vibrational energy of the C=CH_2 functional group is diagnostic for olefin-to-platinum coordination, and the absence of any absorptions at 1647 cm^{-1} indicates there is no on/off process associated with DMBN-to-metal coordination. The infrared spectrum was also determined for the isolated solid of compound **1** in order to detect the metal–chlorine stretch. Only one peak was observed at 330 cm^{-1} which is consistent with the two chlorine atoms being positioned mutually trans to each other,

In comparing the ^1H NMR and ^{13}C NMR data of compounds **1** and **2** some very interesting features are seen. The ^1H NMR of compound **2** is much more complex then that of compound **1** due to the fact that the trigonal-bipyramidal plane of symmetry

(21) Eaborn, C.; Odell, K. J.; Pidcock, A. *J. Chem. Soc., Dalton* **1978**, 357–368.

(22) Krasutskii, P. A.; Yurchenko, A. G.; Rodionov, V. N.; Antipin, M. Yu.; Struchkov, Ya. T. *Teor. Eksp. Khim.* **1983**, *19*, *No. 6*, 685–693.

(23) The structure was carefully modeled using PC-MODEL, Serena Software. All of the Pt to coordinated ligand distances were constrained to their experimentally determined values.

(24) (a) Nakanishi, K.; Solomon, P. H. *Infrared Absorption Spectroscopy*, 2nd ed.; Holden-Day: San Francisco, 1977. (b) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; Wiley: New York, 1972; p 188.

is broken, reducing the point symmetry from C_{2v} to C_s. We were able to distinguish between the protons directed toward the methyl group vs. those directed toward the chlorine atom in compound **2**. All of the olefinic protons directed toward the methyl group apex are upfield from their counterparts presumably because of van der Waals contact shifting. All the resonances associated with protons located on the chlorine side of the trigonal plane are slightly broadened vs. their methyl directed counterparts, attributable we believe to the nuclear quadrupole moment of the chlorine. Most importantly as a result of the lowered symmetry of compound **2**, the coordinated ethylene appears as an AA'BB' pattern with its associated ^{195}Pt satellites. The AA'BB' pattern is reflective of the differential cis, trans coupling across the ethylene double bond for which the constants were determined to be 9.7 and 12.7 Hz, respectively. In both compounds **1** and **2** all Pt–H coupling constants are about 58 Hz.

The proton resonance of ethylene goes through a very distinct upfield chemical coordination shift from its free value of 5.42 to 4.39 ppm in complex **1**. This upfield chemical shift, however, does not occur in DMBN upon coordination. When an axial chlorine atom is replaced by a methyl group, resulting in compound **2**, all olefinic ^{1}H NMR resonances experience an upfield chemical shift. This effect, which is even more dramatic in the ^{13}C NMR, is also observed in the five-coordinate systems involving the bidentate nitrogen ligands.[5d,e]

Coordination of both ethylene and DMBN results in large upfield coordination chemical shifts in compound **1**. This perturbation is a distinct feature of olefin coordination to a metal center[1i,4b,c] and can be used in conjunction with the extant Pt–C coupling constants to ascertain trends in Pt–C bond lengths. Ethylene shows the coordination shift of 67.11 ppm compared to 42.71 ppm for the exocyclic methylene (=CH_2) carbon of DMBN, along with a larger J_{Pt-C} coupling constant of 159.6 Hz vs. 90.3 Hz. This indicates that ethylene is more tightly bound to the platinum center than DMBN, and is reflected in the observed Pt–C bond lengths of 2.154 (7) Å to ethylene vs. 2.254 (5) Å to the exocyclic methylene group to DMBN. The skewness of the DMBN coordination is very nicely shown by the very small 23.38 ppm coordination chemical shift and the correspondingly small 22.0 Hz coupling of the quaternary olefinic carbons (Pt–C = 2.475 (7) Å). It appears certain that the structure of compound **1** in solution is the same as that found in the solid state.

All the trends seen in the ^{13}C NMR data for compound **1** are also observed in compound **2**, although the coordination shifts and Pt–C coupling constants are larger in every instance. Thus replacement of chlorine with the better electron donating methyl group along the trigonal axis (i.e. what may be generically called the σ donor axis) strengthens the binding of the ligands in the trigonal plane. Since there is such a strong preference for π ligands in this region, and the least stable olefin–metal complexes contain electron-donating substituents, the increase in binding would seem to be largely due to increased Pt olefin back-donation. Along with this, all the olefinic carbons in compound **2** display larger platinum–carbon couplings than their counterparts in compound **1**. This is due to substitution of an electron-donating methyl group for a chlorine atom. The methyl group donates electron density to the platinum center which is believed to strengthen the metal-to-olefin backbonding; this is reflected in the upfield chemical shifts and increased J_{Pt-C} coupling constants.

Since for compound **2** only one ethylene carbon resonance is observed (two proton resonances are obligatory for any limiting structure) the coordinated ethylene is required to lie in the trigonal plane of the bipyramidal structure. The NOE distance data also show this in a quantitative way. This fact cannot be determined for the solution structure of compound **1**, although it is found to be true for the solid state.

Although the olefinic resonances of the higher monoolefin compounds **4a–c** and **5** exhibit a coordination chemical shift, these resonances are broadened and often overlap those of DMBN at room temperature. This line broadening is associated with a dynamic process, apparently related to dissociation of these higher olefins. Indeed it has been observed that in the five-coordinate bidentate nitrogen compounds, electron-donating substitutents on the monoolefin decrease the stability of these complexes.[5c-f] Compounds **4a–c** and **5** were cooled to −60 °C. At this temperature all ^{1}H NMR resonances in the olefinic regions were sharpened, which allowed for individual resonance assignments and coupling constant determinations. In the ^{1}H NMR of compounds **4a–c** the DMBN proton resonances closest to methyl substituent groups of each monoolefin display upfield chemical shifts. We attribute this to the van der Waals contact shift in analogy with compound **2**. In compound **5** the very large upfield chemical shifts of some DMBN proton resonances is easily attributed to the fact that they lie within the aromatic ring's shielding cone.

The most important factor that seems to come into play concerning the formation and stability of these five-coordinate complexes, be it with the nitrogen bidentate ligands[5c-e] or with the diene DMBN, is the very unfavorable steric interactions that would occur in the hypothetical four-coordinate square-planar structures through the loss of the monoolefin. Our best frame of reference regarding putative double in-plane square-planar diolefin complexes derives from the crossed diolefin platinum(II) complexes.[25] These are complexes which contain one in-plane and one perpendicular-to-the-plane double bond. It has been found in these four-coordinate complexes that there is a large repulsive cis interaction between the in-plane exocyclic double bond and the neighboring chlorine ligand. This results in the reduction of the Cl–Pt–Cl bond angle to 84.6°. In the present case for the complex to be four coordinate, this unfavorable cis-steric interaction would be approximately doubled. We have created the hypothetical square-planar (DMBN)$PtCl_2$ structure using **1** as a basis (Figure 3) and the rather simple, but plausible, idea that the Cl···Cl and C···Cl repulsions are isoenergetic in the equilibrium geometry. The result is that the Cl–Pt–Cl bond angle is predicted to be 79° and the square-planar structure containing DMBN is stericly less stable than **1** by about 5 kcal. An estimate of the electronic structure preference energy of square-planar over trigonal-bipyramidal geometry of ca. 5 kcal comes from studies of ligand exchange on square-planar platinum in which the pathway is clearly second order.[26] This raises the question of whether increasing the steric bulk of and decreasing the π-accepting character of the third trigonal ligand, so as to promote dissociation, will result in square-planar complexes. This point is under active investigation; however, our current theory on this point is that dissociation of the third in-plane ligand simply leads to solvated five-coordinate complexes.

Summary and Conclusions

It has been found that the diene DMBN is a good promoter of five-coordinate platinum(II) complexes. In these trisolefin complexes all the olefins lie at the equatorial sites, and within the trigonal plane of a trigonal-bipyramidal structure. The important factor that induces this geometry is believed to be the very unfavorable cis steric interactions that would be encountered in the corresponding four-coordinate geometry through loss of the monoolefin.

The following features of these complexes have been observed: (1) Substituting a chlorine atom by a methyl group at the axial site increases the bonding from the metal center to the coordinated olefins by enhancing the π back bonding. (2) Olefin substitution and transmetallation reactions occur slowly with respect to four-coordinate complexes due to increased steric crowding. (3) The presence of electron-donating substitutents on the monoolefin appears to increase the extent and rate of olefin dissociation from the metal center. (4) Access to the four-coordinate square-planar geometry is denied.

Acknowledgement is made to the donors of the Petroleum

(25) (a) Rakowsky, M. H.; Woolcock, J. C.; Wright, L. L.; Green, D. B.; Rettig, M. F.; Wing, R. M. *Organometallics* **1987**, *6*, 1211–1218. (b) Rakowsky, M. H.; Woolcock, J. C.; Rettig, M. F.; Wing, R. M. *Organometallics* **1988**, *7*, 2149–2158.

(26) Haake, P.; Pfeiffer, R. M. *J. Am. Chem. Soc.* **1970**, *92*, 4996.

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Supplementary Material Available: Tables of coordinates, bond distances and angles, best least-squares planes, and torsion angles for **1** (12 pages); listing of structure factors (18 pages). Ordering information is given on any current masthead page.

Phyllanthoside–Phyllanthostatin Synthetic Studies. 7. Total Synthesis of (+)-Phyllanthocin and (+)-Phyllanthocindiol†

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Contribution from the Department of Chemistry, the Laboratory for Research on the Structure of Matter, and the Monell Chemical Senses Center, University of Pennsylvania, Philadelphia, Pennsylvania 19104. *Received June 8, 1990*

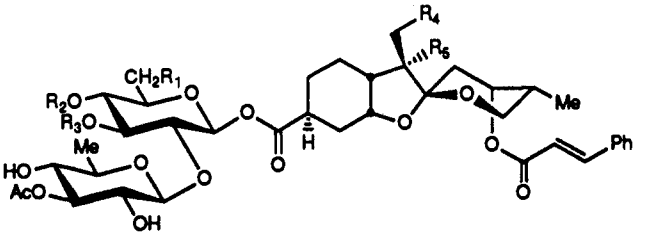
Abstract: A stereochemically linear total synthesis of (+)-phyllanthocin (**5a**), the aglycon methyl ester of the antineoplastic glycoside (+)-phyllanthoside (**1**), is described. The synthesis proceeds in 23 steps (4.5% overall yield) and affords (+)-phyllanthocin in high enantiomeric purity. The central features of the strategy include: (a) construction of aldehyde **8** via a stereoselective, intramolecular ene reaction; (b) elaboration of the spiroketal unit by a two-step tactic involving addition of a functionalized dihydropyran anion (i.e., **9**) to **8**, followed by a highly stereoselective spiroketalization; and (c) chemo- and stereoselective methylenation of the C(7) carbonyl group. In addition, a second-generation approach is presented, wherein an augmented spiroketalization maneuver not only establishes the C(8) spirocenter but also permits the regio- and stereocontrolled introduction of the C(11) methyl group. The latter sequence furnishes (+)-phyllanthocin in 21 steps (5.6% overall yield). Finally, the advanced phyllanthocin intermediate (+)-**49** is converted in five steps (42% overall yield) to (+)-phyllanthocindiol (**5b**), the aglycon of phyllanthostatin 3.

While searching for antitumor agents from the *Euphorbiaceae* family of plants, Kupchan and colleagues isolated (+)-phyllanthoside (**1**), a novel bisabolane glycoside derived from the roots of the Central American tree *Phyllanthus acuminatus* Vahl.[1] Methanolysis of **1** furnished (+)-phyllanthocin (**5a**), a crystalline aglycon methyl ester, whose structure was elucidated in 1977 via single-crystal X-ray analysis.[2] Formulation of the parent glycoside, however, remained unknown until 1982, when Pettit announced the complete characterization of phyllanthoside (**1**) and the closely related phyllanthostatins (**2–4**).[3] The structure of phyllanthocindiol (**5b**), the aglycon of phyllanthostatin 3 (**4**), likewise emerged from X-ray analysis of the derived methyl ester.

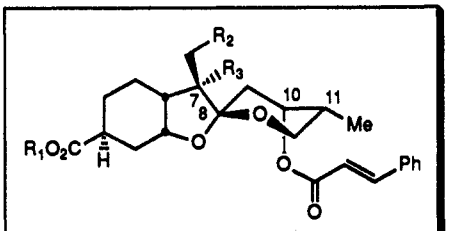
Medicinal interest in these glycosides stems principally from the discovery that phyllanthoside (**1**) and phyllanthostatin 1 (**2**) are potent inhibitors of several NCI tumor cell lines, including human breast cancer and B16 carcinomas.[4] As such both **1** and **2** are currently in phase I clinical trials in the U.K.[4b] Although the aglycon derivative phyllanthocin (**6**) proved to be biologically inactive, it nonetheless has attracted considerable synthetic effort, primarily focused upon the spiroketal architecture.[5-7]

Intrigued with the phyllanthoside–phyllanthostatin class of antitumor agents,[3] we initiated a synthetic program in this area in 1982. Our goals were 4-fold: (a) to develop an efficient synthetic approach to the two aglycons, phyllanthocin (**5a**) and phyllanthocindiol (**5b**); (b) to complete total syntheses of the parent glycoside (+)-phyllanthoside and the closely related phyllanthostatins 1–3; (c) to explore in-depth the chemical reactivity of the [4.5]spiroketal functionality central to the aglycon skeleton; and (d) to prepare a number of structurally related analogues for biological screening.

In this, a full account, we record the realization of the first of these goals, namely an efficient (5.6% and 2.4% overall yields, respectively), stereochemically linear route to (+)-phyllanthocin (**5a**) and (+)-phyllanthocindiol (**5b**) of high enantiomeric purity. From the outset, this venture was seen as prelude to the con-



1 Phyllanthoside: $R_1 = R_2 = H$, $R_3 = Ac$, $R_4, R_5 = O$ (epoxide)
2 Phyllanthostatin 1: **1**, $R_2 = Ac$, $R_3 = H$
3 Phyllanthostatin 2: **1**, $R_1 = OH$
4 Phyllanthostatin 3: **1**, $R_4 = R_5 = OH$



5a Phyllanthocin: $R_1 = Me$, $R_2, R_3 = O$ (epoxide)
5b Phyllanthocindiol: $R_1 = H$, $R_2 = R_3 = OH$

† This paper is dedicated to the memory of Dr. Mineo Fukui.
‡ Deceased, Aug 14, 1990.

(1) Watt, J. M.; Breyer-Brandwijk, M. G. *The Medicinal and Poisonous Plants of Southern and Eastern Africa*; E. S. Livingstone Ltd: London, 1962; p 426. Morton, J. F. *Major Medicinal Plants*; C. C. Thomas: Springfield, IL, 1977; pp 193, 366.

0002-7863/91/1513-2071$02.50/0