Synthesis and Structure of Isomeric Palladium(II)−Pyrazole Chelate Complexes with and without an N−H Group as Hydrogen Bond Donor

Douglas B. Grotjahn,* David Combs, and Sang Van

Department of Chemistry, San Diego State University, 5500 Campanile Drive, San Diego, California 92182-1030

Gerardo Aguirre and Fernando Ortega

Centro de Graduados e Investigación, Instituto Technológico de Tijuana, Apartado Postal 1166, 22000 Tijuana, Baja California, Mexico

Received August 18, 1999

Four new ligands containing a pyrazole ring and either a phosphine or thioether were prepared and converted to their *cis*-dichloropalladium(II) complexes. Two of the ligands are especially notable for the attachment of a side chain at pyrazole carbon, rather than at nitrogen. The new metal complexes include dichloro[3-(diphenylphosphinomethyl)pyrazole]palladium(II) (**1**-$PdCl_2$) and dichloro[3-(methylthiomethyl)pyrazole]palladium(II) (**2**-$PdCl_2$), which both feature an N−H group as a potential proton or hydrogen bond donor. For comparison, isomeric complexes lacking an NH group were prepared: dichloro[1-(diphenylphosphinomethyl)pyrazole]palladium(II) (**3**-$PdCl_2$) and dichloro[1-(methylthiomethyl)pyrazole]palladium(II) (**4**-$PdCl_2$). As determined by X-ray crystallography, all four complexes were found to have slightly distorted square planar geometry. Complexes **1**-$PdCl_2$ and **2**-$PdCl_2$, which contain an NH group, exhibit both intermolecular and intramolecular hydrogen bonding, whereas isomers **3**-$PdCl_2$ and **4**-$PdCl_2$ do not. Single-crystal X-ray structure determinations on the following compounds are reported: **1**-$PdCl_2$, space group $P\bar{1}$, $a = 8.4488(9)$ Å, $b = 8.9175(13)$ Å, $c = 12.731(2)$ Å, $Z = 2$, $V = 871.8(2)$ Å^3; **2**-$PdCl_2$, space group *Pbca*, $a = 10.8827(10)$ Å, $b = 11.7721(7)$ Å, $c = 14.874(2)$ Å, $Z = 8$, $V = 1905.6$ Å^3; **3**-$PdCl_2$, space group $P2_1/c$, $a = 20.520(2)$ Å, $b = 12.549(2)$ Å, $c = 13.9784(13)$ Å, $Z = 8$, $V = 3401.1(6)$ Å^3; **4**-$PdCl_2$, space group *Pbca*, $a = 10.6545(10)$ Å, $b = 12.0205(11)$ Å, $c = 14.6474(14)$ Å, $Z = 8$, $V = 1875.9(3)$ Å^3.

Introduction

Many metalloenzymes activate substrates using a combination of one or more metal ions and nearby functional groups capable of donating or accepting one or more hydrogen bonds or protons.[1,2] In recent years, a variety of artificial metal−ligand complexes have been prepared to study the effects of such cooperativity on reactions as diverse as the hydrolysis of phosphate esters[3] and carboxylic acid amides,[4] the heterolysis of dihydrogen,[5] or the interaction of dioxygen and hemes.[6]

Pyrazole complexes have not been studied in this context. However, very limited literature data on the acidifying effect of metal complexation suggest that suitably designed pyrazole complexes should allow the study of cooperativity between metal ions and proton donors or acceptors at near-physiological pH: the free ligand exhibits a pK_a of 14.2,[7] whereas pyrazole complexes of $Cr^{III}(NH_3)_5$, $Co^{III}(NH_3)_5$, and $Ru^{III}(NH_3)_5$ have pK_a values in the range 5.98−7.21.[8]

In order to anchor a metal ion firmly on a pyrazole derivative, we have designed polydentate ligands (**1** and **2**, Scheme 1) to form stable chelates involving one soft ligating atom (P or S) and one pyrazole N, while leaving the other pyrazole N and its attached hydrogen available for donating a hydrogen bond or a proton to another ligand on the metal. Although hundreds of polydentate ligands containing pyrazoles are known,[9] virtually all of them feature a pyrazole ring substituted at one nitrogen, probably because of the ease of synthesizing such systems. For

* Correspondence author. E-mail: grotjahn@sundown.sdsu.edu.

(1) Lippard, S. J.; Berg, J. M. *Principles of Bioinorganic Chemistry*; University Science Books: Mill Valley, CA, 1994; pp 257−281.
(2) For a discussion of carboxypeptidase, see: Creighton, T. E. *Proteins: Structures and Molecular Properties*, 2nd ed.; W. H. Freeman: New York, 1993; pp 431−434.
(3) Leading references: (a) Wall, M.; Linkletter, B.; Williams, D.; Lebuis, A.-M.; Hynes, R. C.; Chin, J. *J. Am. Chem. Soc.* **1999**, *121*, 4710−4711. (b) Kövári, E.; Krämer, R. *J. Am. Chem. Soc.* **1996**, *118*, 12704−12709. (c) Kimura, E.; Kodama, Y.; Koike, T.; Shiro, M. *J. Am. Chem. Soc.* **1995**, *117*, 8304−8311. (d) Morrow, J. R.; Aures, H.; Epstein, D. *J. Chem. Soc., Chem. Commun.* **1995**, 2431−2432. (e) Chu, F.; Smith, J.; Lynch, V. M.; Anslyn, E. V. *Inorg. Chem.* **1995**, *34*, 5689−5690. (f) Suh, J. *Acc. Chem. Res.* **1992**, *25*, 273−279. (g) Breslow, R.; Berger, D.; Huang, D.-L. *J. Am. Chem. Soc.* **1990**, *112*, 3686−3687.
(4) Leading references: (a) Schepartz, A.; Breslow, R. *J. Am. Chem. Soc.* **1987**, *109*, 1814−1826. (b) Groves, J. T.; Baron, L. A. *J. Am. Chem. Soc.* **1989**, *111*, 5442−5448.
(5) (a) Lee, D.-H.; Patel, B. P.; Clot, E.; Eisenstein, O.; Crabtree, R. H. *Chem. Commun. (Cambridge)* **1999**, 297−298. (b) Lee, J. C., Jr.; Peris, E.; Rheingold, A. L.; Crabtree, R. H. *J. Am. Chem. Soc.* **1994**, *116*, 11014−11019. (c) Lough, A. J.; Park, S.; Ramachandran, R.; Morris, R. H. *J. Am. Chem. Soc.* **1994**, *116*, 8356−8357.
(6) Momenteau, M.; Reed, C. A. *Chem. Rev.* **1994**, *94*, 659−698.
(7) Yagil, G. *Tetrahedron* **1967**, *23*, 2855−2861.
(8) Johnson, C. R.; Henderson, W. W.; Shepherd, R. E. *Inorg. Chem.* **1984**, *23*, 2754−2763. Winter, J. A.; Caruso, D.; Shepherd, R. A. *Inorg. Chem.* **1988**, *27*, 1086−1089.
(9) Trofimenko, S. *Chem. Rev.* **1993**, *93*, 943−980. See also: Sadimenko, A. P.; Basson, S. S. *Coord. Chem. Rev.* **1996**, *147*, 247−297.

10.1021/ic990995q CCC: $19.00
Published on Web 04/21/2000

Scheme 1

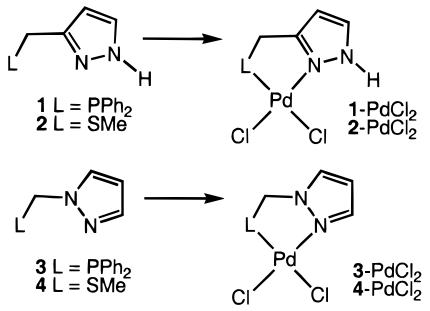
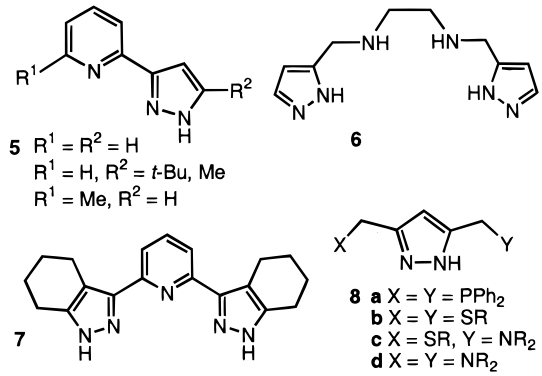


Chart 1



example, deprotonation of pyrazole and subsequent reaction with an alkyl halide lead to an N-alkylated pyrazole, and one-step reaction of a borohydride salt and the appropriate amount of a pyrazole derivative creates a poly(pyrazolyl)borate ion, where anywhere from one to four pyrazolyl groups can be incorporated. However, these and all other N-substituted pyrazole derivatives are unsuitable for our purpose because, after complexation to the remaining unsubstituted nitrogen atom, neither nitrogen is available for proton- or hydrogen-bond acceptance. Therefore, in this study, a pyrazole substituent containing a ligating P or S atom must be attached to a *carbon* of the heterocycle. The surprisingly few such compounds which have been prepared and coordinated to transition metals are portrayed in Chart 1.[10] Compounds **8a**−**c** feature soft ligating atoms but readily form binuclear complexes with a bridging pyrazolate ligand, an undesirable situation in our work. Therefore, here new ligands **1** and **2** featuring one pyrazole ring substituted at carbon with a single $-CH_2SCH_3$ or $-CH_2PPh_2$ group are reported, along with their square-planar, mononuclear complexes to a *cis*-dichloropalladium(II) fragment. Finally, for comparative purposes isomeric ligands (**3** and **4**) and complexes without an NH group are also presented.

Experimental Section

General. Unless otherwise specified, ^{1}H, ^{13}C, and ^{31}P data were measured at room temperature on a 200 MHz (50.3 MHz for ^{13}C and 81.0 MHz for ^{31}P) or nominal 500 MHz (499.9 MHz for ^{1}H, 125.7 MHz for ^{13}C) spectrometer. ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million downfield from tetramethylsilane and referenced to residual solvent resonances (^{1}H NMR, 7.27 for C*H*Cl$_3$ and 2.50 for C*H*D$_2$SOCD$_3$; ^{13}C NMR, 77.23 for *C*DCl$_3$ and 39.51 for for CD$_3$SO*C*D$_3$), where ^{1}H NMR chemical shifts are followed by multiplicity, coupling constants *J* in hertz, and integration in parentheses. For complex coupling patterns, e.g., "(dt, J = 3.2, 7.6, 1H)", the first doublet (d) represents the smaller coupling, and the second triplet (t) indicates the larger coupling. In some compounds, a doublet of doublets (dd) in ^{1}H NMR for the pyrazole protons is reported as an apparent triplet (app t) due to the signal appearance. Assignments are provided for key moieties only. ^{31}P{^{1}H} NMR chemical shifts are referenced to external 85% H_3PO_4 (aq).

IR spectra were obtained on a Perkin-Elmer 1600 FTIR spectrometer. Samples were prepared either neat (NaCl plates) or in a solid (KBr pellets), and absorptions are reported in wavenumbers (cm^{-1}). Elemental analyses were performed at NuMega Resonance Labs, San Diego, CA.

Chromatography was carried out with a Harrison Research Chromatotron under N_2 atmosphere; silica gel (SiO_2) and deoxygenated solvents were used.

Bis(acetonitrile)palladium(II) dichloride was either purchased or prepared in a manner similar to that reported for the benzonitrile analogue.[11]

3-(Diphenylphosphinomethyl)pyrazole (1). To a solution of THF (50 mL) and triphenylphosphine (1.011 g, 3.86 mmol) at room temperature was added lithium (0.0533 g, 7.68 mmol), and after 2 h of stirring the lithium had dissolved. The bright red solution was cooled to 0 °C, and 3-(chloromethyl)pyrazole hydrochloride (**12**) (0.1942 g, 1.26 mmol) was added at once as a solid. The ice bath was removed and the reaction solution was stirred for an additional 2 h. Deoxygenated water (25 mL) was added to the reaction mixture followed by deoxygenated Et_2O (50 mL). The organic phase was separated and the aqueous phase extracted with deoxygenated Et_2O (2 × 25 mL). The organic phases were combined and dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by chromatography (SiO_2, 50% ethyl acetate/petroleum ether) to give **1** (0.246 g, 0.92 mmol, 73%) as a clear colorless air-sensitive oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.50−7.43 (m, 4 H), 7.41 (d, J = 2.0 Hz, 1 H), 7.37−7.25 (m, 6 H), 5.99 (d, J = 2.0 Hz, 1 H), 3.47 (s, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125.7 MHz): δ 144.52, 138.16 (d, J = 14.3 Hz), 134.13, 132.97 (d, J = 18.6 Hz), 129.11, 128.73 (d, J = 6.6 Hz), 105.18 (d, J = 5.1 Hz), 27.14 (d, J = 6.2 Hz) ppm. ^{31}P{^{1}H} ($CDCl_3$, 81.0 MHz): δ −14.45 ppm. IR (neat, NaCl) 3179, 3060, 2976, 2924, 1480, 1433 cm^{-1}.

***cis*-Dichloro[3-(diphenylphosphinomethyl)pyrazole]palladium-(II) (1-PdCl$_2$).** To **1** (0.124 g, 0.46 mmol) and bis(acetonitrile)-palladium(II) dichloride (0.121 g, 0.46 mmol) was added deoxygenated methanol (10 mL). The reaction slurry was stirred for 14 h at room temperature. The reaction slurry was filtered, and the solid was washed with CH_2Cl_2 (2 × 10 mL). The solid residue was placed under vacuum to give **1**-PdCl$_2$ (0.192 g, 0.43 mmol, 93%) as a yellow solid. Slow evaporation of methanol from a dilute solution of **1**-PdCl$_2$ in methanol afforded crystals suitable for X-ray analysis. ^{1}H NMR (DMSO-d_6, 200 MHz): δ 12.90 (s, 1 H), 7.88 (m, 5 H), 7.60 (m, 6 H), 6.54 (bs, 1 H), 4.03 (d, J = 13 Hz, 2 H) ppm. ^{13}C{^{1}H} NMR (DMSO-d_6, 50.3 MHz): δ 152.38 (d, J = 6.5 Hz), 134.09, 133.09 (d, J = 11.0 Hz), 132.28 (d, J = 3.1 Hz), 129.14 (d, J = 11.8 Hz), 127.67 (d, J = 55.4 Hz), 104.56 (d, J = 12.9 Hz), 28.68 (d, J = 31.9 Hz) ppm. ^{31}P{^{1}H} NMR (DMSO-d_6, 81.0 MHz): δ 46.67 ppm. IR (KBr): 3286, 3170, 3047, 2937, 1509, 1434, 1199, 1109 cm^{-1}. Anal. Calcd for $C_{16}H_{15}Cl_2N_2PPd$ (443.60): C, 43.32; H, 3.41; N, 6.31. Found: C, 43.19; H, 3.27; N 6.02.

3-(Methylthiomethyl)pyrazole (2). 3-(Chloromethyl)pyrazole hydrochloride (**12**) (1.77 g, 11.6 mmol) was partially dissolved in THF (100 mL) under a nitrogen atmosphere. At room temperature, lithium thiomethoxide (1.25 g, 23.2 mmol) was added to the mixture. The reaction mixture became slightly pink. The reaction slurry was stirred for 10 h and quenched with water (3 mL). The organic phase was extracted with ethyl acetate (3 × 10 mL). The organic phases were

(10) (a) Deters, R.; Krämer, R., *Inorg. Chim. Acta* **1998**, *269*, 117−124. (b) Singh, K.; Long, J. R.; Stavropoulos, P., *Inorg. Chem.* **1998**, *37*, 1073−1079. (c) Zadycowicz, J.; Potvin, P. G., *J. Org. Chem.* **1998**, *63*, 235−240. (d) Meyer, F.; Ruschewitz, U.; Schober, P.; Antelmann, B.; Zsolnai, L. *J. Chem. Soc., Dalton Trans.* **1998**, 1181−1186. (e) Satake, A.; Nakata, T. *J. Am. Chem. Soc.* **1998**, *120*, 10391−10396. (f) Ward, M. D.; Fleming, J. S.; Psillakis, E.; Jeffery, J. C.; McCleverty, J. A. *Acta Crystallogr., Sect. C* **1998**, *C54*, 609−612. (g) Meyer, F.; Jacobi, A.; Zsolnai, L. *Chem. Ber./Recueil* **1997**, *130*, 1441−1447. (h) Schenck, T. G.; Downes, J. M.; Milne, C. R. C.; Mackenzie, P. B.; Boucher, H.; Whelan, J.; Bosnich, B. *Inorg. Chem.* **1985**, *24*, 2334−2337.

(11) Doyle, J. R.; Slade, P. E.; Jonassen, H. B. *Inorg. Synth.* **1960**, *6*, 216−219.

combined, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by Kugelrohr distillation at 140 °C under oil pump vacuum to **2** (1.22 g, 9.52 mmol, 82%) as a clear oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.20 (bs, 1 H), 7.55 (d, J = 2.5 Hz, 1 H), 6.24 (d, J = 2.5 Hz, 1 H), 3.77 (s, 2 H), 2.06 (s, 3 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125.7 MHz): δ 146.31, 132.85, 104.78, 30.08, 15.42 ppm. IR (neat, NaCl): 3180, 3163, 2971, 2910, 1571, 1529, 1468, 1432, 1143, 1101, 1054, 981, 783 cm^{-1}.

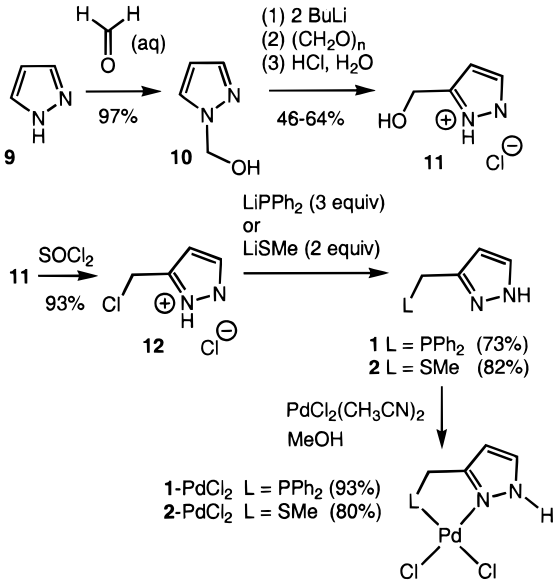
***cis*-Dichloro[3-(methylthiomethyl)pyrazole]palladium(II) (2-PdCl$_2$).** To a solution of **2** (0.67 g, 5.25 mmol) in methanol (10 mL) under nitrogen atmosphere was added at room temperature bis(acetonitrile)palladium(II) dichloride (1.36 g, 5.25 mmol). The palladium complex was dissolved in 5 min with stirring. After 12 h of stirring, an orange precipitate formed. The reaction mixture was filtered, and the solid was washed with methanol (2 × 5 mL). The solid residue was placed under vacuum to give **2**-$PdCl_2$ (1.36 g, 4.46 mmol, 80%) as a yellow solid. Crystals suitable for X-ray analysis were grown from the diffusion of acetone into a solution of **2**-$PdCl_2$ in DMSO. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.5 (s, 1 H), 7.89 (d, J = 2.0 Hz, 1 H), 6.54 (d, J = 2.0 Hz, 1 H), 4.31 (d, J = 16.5 Hz, 1 H), 3.99 (d, J = 16.5 Hz, 1 H), 2.62 (s, 3 H) ppm. ^{13}C{^{1}H} (DMSO-d_6, 125.7 MHz): δ 154.92, 133.44, 104.61, 35.06, 23.15 ppm. IR (KBr): 3329, 3129, 2921, 2850, 1511, 1420, 1371, 778 cm^{-1}. Anal. Calcd for $C_5H_8Cl_2N_2PdS$ (305.52): C, 19.66; H, 2.64; N, 9.17. Found: C, 19.39; H, 2.34; N, 8.94.

1-(Diphenylphosphinomethyl)pyrazole (3). Diphenylphosphine (2.642 g, 14.2 mmol) was placed into a Schlenk flask with degassed THF (50 mL). The solution was cooled to −78 °C, and *n*-butyllithium (8.4 mL, 1.6 M in hexanes, 15.0 mmol) was added dropwise. The red solution was stirred at −78 °C for an additional 1 h. The ice bath was removed, and the solution was stirred for an additional 3 h. The red solution was cooled to 0 °C, and **13** (0.698 g, 4.56 mmol) was added at once as a solid. The ice bath was removed, and the reaction mixture was stirred for 11 h before addition of deoxygenated methanol (25 mL) and water (20 mL). The organic phase was separated, and the aqueous phase was extracted with deoxygenated Et_2O (3 × 10 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated. The crude material was purified by chromatography (SiO_2, 10% ethyl acetate/petroleum ether) to give **3** (0.574 g, 2.16 mmol, 47%) as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.49 (dd, J = 2.0, 0.5 Hz, 1 H), 7.45−7.40 (m, 4 H), 7.40−7.35 (m, 6 H), 7.25 (dd, J = 2.5, 0.5 Hz, 1 H), 6.19 (dd, J = 2.5, 2.0 Hz, 1 H), 4.91 (d, J = 4.5 Hz, 2 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125.7 MHz): δ 139.50, 136.04 (d, J = 13.4 Hz), 133.18 (d, J = 19.3 Hz), 129.34, 129.49, 128.95 (d, J = 6.4 Hz), 106.11, 53.01 (d, J = 16.0 Hz) ppm. ^{31}P{^{1}H} NMR ($CDCl_3$, 81.0 MHz): δ −14.98 ppm. IR (KBr): 3129, 3111, 3107, 3069, 3049, 3025, 3015, 3002, 2969, 2905, 1427, 1386, 1089, 1042 cm^{-1}. Anal. Calcd for $C_{16}H_{15}N_2P$ (266.28): C, 72.17; H, 5.68; N, 10.52. Found: C, 72.04; H, 5.56; N, 10.28.

***cis*-Dichloro[1-(diphenylphosphinomethyl)pyrazole]palladium(II) (3-PdCl$_2$).** A flask was charged with **3** (0.049 g, 0.184 mmol) and bis(acetonitrile)palladium(II) dichloride (0.048 g, 0.186 mmol). Deoxygenated methanol (5 mL) was added. The resulting yellow solution instantaneously became cloudy. The slurry was stirred for 5 h at room temperature and then filtered through a glass frit. The precipitate was washed with CH_2Cl_2 and then dried under vacuum (0.05 mmHg), giving **3**-$PdCl_2$ (0.068 g, 0.153 mmol, 83%) as a yellow solid. Crystals suitable for X-ray analysis were grown from the slow evaporation from a solution of **3**-$PdCl_2$ in CH_2Cl_2. ^{1}H NMR (DMSO-d_6, 200 MHz): δ 8.26−8.22 (m, 1 H), 8.12−8.08 (m, 1 H), 8.00−7.80 (m, 4 H), 7.75−7.40 (m, 6 H), 6.63−5.99 (m, 1 H), 5.47 (d, J = 8.2 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 125.7 MHz): δ 141.50, 133.68, 133.43 (d, J = 11.4 Hz), 132.93 (d, J = 3.0 Hz), 129.39 (d, J = 12.0 Hz), 125.98 (d, J = 58.4 Hz), 108.67, 49.98 (d, J = 37.6 Hz); ^{31}P{^{1}H} NMR ($CDCl_3$, 81.0 MHz): δ 43.43 ppm. IR (KBr): 3117, 3036, 2933, 2899, 2841, 1434, 1405, 1101 cm^{-1}. Anal. Calcd for $C_{16}H_{15}Cl_2N_2PPd$ (443.60): C, 43.32; H, 3.41; N, 6.31. Found: C, 43.54; H, 3.40; N, 6.06.

1-(Methylthiomethyl)pyrazole (4). Method A. 1-(Chloromethyl)-pyrazole hydrochloride (**13**) (2.00 g, 13.0 mmol) was mixed with dry THF (100 mL), and lithium thiomethoxide (1.40 g, 26.0 mmol) was added at room temperature. The reaction slurry was stirred for 12 h and quenched with water (3 mL). The organic phase was extracted with ethyl acetate (3 × 10 mL). The organic phases were combined, dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by Kugelrohr distillation at 60−70 °C under oil-pump vacuum to give **4** (1.67 g, 11.7 mmol, 70%) as a yellow oil.

Scheme 2



Method B. Pyrazole (**9**) (2.00 g, 29.0 mmol) was dissolved in THF (20 mL), and the reaction solution was cooled to 0 °C. Sodium hydride (0.70 g, 29.0 mmol) was slowly added. After the bubbling ceased, (chloromethyl)methyl sulfide (2.80 g, 29.0 mmol) was added at 0 °C and the reaction mixture was warmed to room temperature by removal of the ice bath. The reaction slurry was stirred for an additional 30 min before it was concentrated. The crude mixture was purified as described in method A to give the **4** (1.72 g, 13.3 mmol, 46%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.58 (d, J = 2 Hz, 1 H), 7.51 (d, J = 1.5 Hz, 1 H), 6.32 (app t, J = 2.0 Hz, 1 H), 5.15 (s, 2 H), 2.12 (s, 3 H) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 125.7 MHz): δ 139.79, 128.94, 106.87, 54.79, 15.03 ppm. IR (neat, NaCl): 3103, 2983, 2923, 1510, 1432, 1083, 1047, 964, 752 cm^{-1}.

***cis*-Dichloro[1-(methylthiomethyl)pyrazole]palladium(II) (4-PdCl$_2$).** To a solution of **4** (0.160 g, 1.25 mmol) in methanol (10 mL) was added bis(acetonitrile)palladium(II) dichloride (0.325 g, 1.25 mmol) at room temperature. The reaction was stirred for 12 h, during which time a yellow precipitate formed. The reaction mixture was filtered, and the solid was washed with methanol (2 × 5 mL). The solid residue was placed under vacuum to give pure **4**-$PdCl_2$ (0.297 g, 0.98 mmol, 78%) as a yellow solid. Crystals suitable for X-ray analysis were grown from the diffusion of acetone into a solution of **4**-$PdCl_2$ in DMSO. ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.33−8.30 (m, 1 H), 7.92−7.89 (m, Hz, 1 H), 6.63−6.60 (m, 1 H), 5.51 (d, J = 12.5 Hz, 2 H), 5.38 (d, J = 12.5 Hz, 2 H), 2.53 (s, 3 H). ^{13}C{^{1}H} (DMSO-d_6, 125.7 MHz): δ 141.44, 134.32, 108.15, 54.83, 21.16. IR (KBr): 3120, 2975, 2915, 1404, 1278, 1056, 767 cm^{-1}. Anal. Calcd for $C_5H_8Cl_2N_2PdS$ (305.52): C, 19.66; H, 2.64; N, 9.17. Found: C, 19.42; H, 2.34; N, 8.88.

3-(Hydroxymethyl)pyrazole hydrochloride (11) is a known compound,[12] but this is a new procedure for making it. To a solution of 1-(hydroxymethyl)pyrazole (3.49 g, 35.6 mmol) in THF (150 mL) was added a solution of *n*-BuLi in hexanes (32 mL, 2.5 M, 80.0 mmol) at −78 °C. After addition was completed, a white precipitate formed. The reaction slurry was warmed to −20 °C for 2 h before the addition of paraformaldehyde (1.34 g, 44.5 mmol). The reaction slurry was warmed to room temperature and stirred for 10 h, after which time 2 N HCl (aq) was added until the pH of the mixture reached 4. After stirring for 4 h, the solution was neutralized with saturated $NaHCO_3$ (aq) until the pH of the mixture reached 7−8. The solvents were removed by

(12) Jones, R. G. *J. Am. Chem. Soc.* **1949**, *71*, 3994−4000.

Table 1. Crystallographic Data for **1**-$PdCl_2$, **2**-$PdCl_2$, **3**-$PdCl_2$, and **4**-$PdCl_2$

	1-$PdCl_2$	**2**-$PdCl_2$
empirical formula	$C_{16}H_{15}Cl_2N_2PPd$	$C_5H_8Cl_2N_2PdS$
fw	443.57	305.49
temp	291(2) K	294(2) K
wavelength	0.71073 Å	0.71073 Å
cryst syst	triclinic	orthorhombic
space group	$P\bar{1}$	*Pbca*
unit cell dimens	$a = 8.4488$ (9) Å , $\alpha = 97.758$ (13)°	$a = 10.8827(10)$ Å, $\alpha = 90°$
	$b = 8.9175$ (13) Å, $\beta = 93.558(10)°$	$b = 11.7721(7)$ Å, $\beta = 90°$
	$c = 12.731$ (2) Å, $\gamma = 112.409$ (9)°	$c = 14.874(2)$ Å, $\gamma = 90°$
vol	871.8(2) $Å^3$	1905.6 $Å^3$
Z and $F(000)$	2 and 440	8 and 1184
density (calcd)	1.690 Mg/m^3	2.130 Mg/m^3
abs coeff	1.459 mm^{-1}	2.666 mm^{-1}
abs corr	none	semiempirical from ψ-scans
cryst size	0.38 × 0.35 × 0.12 mm	0.60 × 0.50 × 0.40
θ range for data collection	1.63−25.00°	2.74−30.00°
scan type and scan width	$2\theta-\theta$ and $K_{\alpha^1} - 1°$ to $K_{\alpha^2} + 1°$	$2\theta-\theta$ and $K_{\alpha^1} - 1°$ to $K_{\alpha^2} + 1°$
scan time/background time	2:1	2:1
index ranges	$-1 \le h \le 9, -10 \le k \le 10, -15 \le l \le 15$	$0 \le h \le 15, 0 \le k \le 16, 0 \le l \le 20$
reflns collected	3747	2785
indep reflns	3066 ($R_{int} = 0.0295$)	2785
max and min transm		0.3129 and 0.2335
refinement meth	full-matrix least squares on F^2	full-matrix least squares on F^2
data/restraints/params	3063/0/199	2782/0/100
goodness of fit on F^2, (S)	1.081	0.998
final R indices [$I>2\sigma(I)$]	R1 = 0.0298, wR2 = 0.0736	R1 = 0.0358, wR2 = 0.0917
R indices (all data)	R1 = 0.0403, wR2 = 0.0972	R1 = 0.0554, wR2 = 0.1189
largest diff peak and hole	0.433 and −0.429 e $Å^{-3}$	1.070 and −0.602 e $Å^{-3}$

	3-$PdCl_2$	**4**-$PdCl_2$
empirical formula	$C_{16}H_{15}Cl_2N_2PPd$	$C_5H_8Cl_2N_2PdS$
fw	443.57	305.49
temp	294(2) K	294(2) K
wavelength	0.71073 Å	0.71073 Å
cryst sys	monoclinic	orthorhombic
space group	$P2_1/c$	*Pbca*
unit cell dimens	$a = 20.520$ (2) Å, $\alpha = 90°$	$a = 10.6545$ (10) Å, $\alpha = 90°$
	$b = 12.549$ (2) Å, $\beta = 109.112$ (7)°	$b = 12.0205$ (11) Å, $\beta = 90°$
	$c = 13.9784$ (13) Å, $\gamma = 90°$	$c = 14.6474$ (14) Å, $\gamma = 90°$
vol	3401.1(6) $Å^3$	1875.9(3) $Å^3$
Z and $F(000)$	8 and 1760	8 and 1184
density (calcd)	1.733 Mg/m^3	2.163 Mg/m^3
abs coeff	1.496 mm^{-1}	2.708 mm^{-1}
abs corr	semiempirical from ψ-scans	semiempirical from ψ-scans
cryst size	0.50 × 0.45 × 0.32 mm	0.45 × 0.35 × 0.28 mm
θ range for data collection	2.10−25.00°	2.78−30.00°
scan type and scan width	$2\theta-\theta$ and $K_{\alpha^1} - 1°$ to $K_{\alpha^2} + 1°$	$2\theta-\theta$ and $K_{\alpha^1} - 1°$ to $K_{\alpha^2} + 1°$
scan time/background time	2:1	2:1
index ranges	$-24 \le h \le 23, -14 \le k \le 0, 0 \le l \le 16$	$0 \le h \le 14, 0 \le k \le 16, 0 \le l \le 20$
reflns collected	6264	2743
indep reflns	5992 ($R_{int} = 0.0425$)	2743
max and min transm	0.4197 and 0.3506	0.3575 and 0.2019
refinement meth	full-matrix least squares on F^2	full-matrix least squares on F^2
data/restraints/params	5985/0/397	2742/0/100
goodness of fit on F^2, (S)	1.020	1.07
final R indices [$I>2\sigma(I)$]	R1 = 0.0559, wR2 = 0.1127	R1 = 0.0356, wR2 = 0.0937
R indices (all data)	R1 = 0.1250, wR2 = 0.1496	R1 = 0.0447, wR2 = 0.1024
largest diff peak and hole	0.707 and −0.666 e $Å^{-3}$	0.715 and −1.640 e $Å^{-3}$

rotary evaporation, leaving a thick oil, which was subjected to Kugelrohr distillation under vacuum (0.05 mmHg, 120−140 °C), affording a clear colorless oil, which was dissolved in methanol (2 mL). Concentrated HCl (aq) was added. After 15 min, solvents were removed by rotary evaporation and the resulting solid residue was redissolved in methanol (2 mL), followed by the addition of diethyl ether (10 mL), which caused a white precipitate to form. The white precipitate was collected by vacuum filtration and dried under vacuum to yield 3-(hydroxymethyl)-pyrazole hydrochloride (2.20 g, 46%).

Results and Discussion

Synthesis and Properties of 3-Phosphino- and 3-Thiomethyl Pyrazole Palladium(II) Dichlorides. To introduce a functionalized side chain at carbon of the pyrazole ring, first the acidic pyrazole NH function was protected with a group which would also direct deprotonation of the pyrazole ring with strong base. Katritzky and co-workers[13] have previously reported the synthesis of 1-hydroxymethylpyrazole (**10**, Scheme 2) from pyrazole (**9**) and aqueous formaldehyde in THF. We have found that organic solvent was unnecessary; moreover, the yield of **10** exceeded 95%. Protected pyrazole **10** was then lithiated as reported with 2 equiv of *n*-butyllithium.[13] We found that the resulting species generated in situ could be hydroxyalkylated with formaldehyde. Subsequent deprotection in aqueous hydrochloric acid gave 3-hydroxymethylpyrazole[12] as its hydrochloride salt **11** in 46−64% yield. Conversion of the alcohol

(13) Katritzky, A. R.; Lue, P.; Akutagawa, K. *Tetrahedron* **1989**, *45*, 4243−4262.

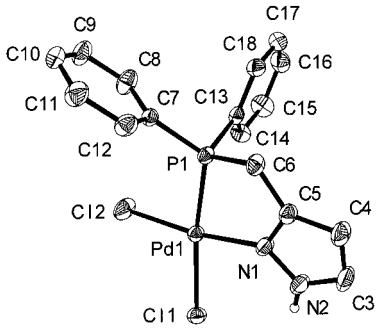


Figure 1. Molecular structure of **1**-$PdCl_2$.

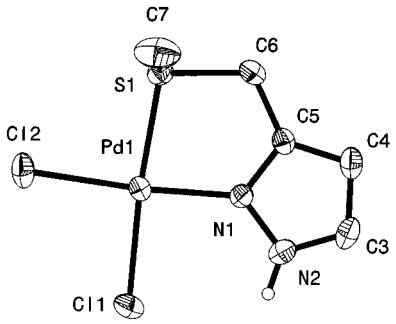


Figure 2. Molecular structure of **2**-$PdCl_2$.

functional group in **11** to a chloride in **12** was accomplished with thionyl chloride[12] in 93% yield.

Using a procedure similar to that reported by Bosnich[10h] and co-workers for the preparation of 1,3-bis(diphenylphosphinomethyl)pyrazole (**8a**) from 1,3-bis(chloromethyl)pyrazole hydrochloride salt and excess lithium diphenylphosphide, we were able to obtain the desired phosphine ligand **1** in 73% yield using 3 equiv of $LiPPh_2$ and 3-chloromethylpyrazole hydrochloride. In addition, thioether ligand **2** could be prepared in 82% yield by treatment of chloride **12** with 2 equiv of LiSMe. The Ph_2-PCH_2 side chain in ligand **1** was identified by a singlet in the $^{31}P\{^1H\}$ NMR spectrum at −14.45 ppm and a carbon doublet in the $^{13}C\{^1H\}$ NMR spectrum at 27.14 ppm, while the $MeSCH_2$ side chain in **2** was identified by two singlets in the ^1H NMR spectrum at 2.06 and 3.77 ppm, ascribed to the methyl and methylene protons, respectively.

Pyrazole ligands **1** and **2** were cleanly complexed to the $PdCl_2$ fragment in yields of 93% and 80%, respectively (Scheme 2). The ^1H NMR spectra of **1**-$PdCl_2$ and **2**-$PdCl_2$ exhibit slightly broad singlets at 12.90 and 12.50 ppm, respectively, verifying the anticipated lack of oxidative addition of the pyrazole N−H bond to Pd(II). Complexation of phosphorus to palladium in complex **1**-$PdCl_2$ was indicated by a signal at 46.67 ppm in the $^{31}P\{^1H\}$ NMR spectrum, significantly downfield of the chemical shift shown by the free phosphine. Finally, complex **2**-$PdCl_2$ was easily identified by two mutually coupled doublets (3.99 and 4.31 ppm, $J = 16.5$ Hz) in its ^1H NMR spectrum, ascribed to two diastereotopic protons on the methylene carbon.

Crystals of the two complexes suitable for X-ray diffraction were grown in the case of **1**-$PdCl_2$ by the slow evaporation of methanol at room temperature and for **2**-$PdCl_2$ by the diffusion of acetone into a DMSO solution of the complex. The solid state structures of **1**-$PdCl_2$ and **2**-$PdCl_2$ were solved as described in Table 1, and the ORTEP views of both complexes from above the square plane are shown in Figures 1 and 2. Figures 3 and 4 provide views of the closest *intermolecular* hydrogen bonds for the two complexes.

Palladium dichloride complex **1**-$PdCl_2$ is a slightly distorted square planar complex with the sum of four angles around the palladium equal to 359.9(1)°. Selected bond lengths and angles are shown in Table 2. The distance between Pd and the Cl trans to P [Cl(1), 2.3941(10) Å] is about 0.11 Å longer than the Pd−Cl(2) bond length, presumably because of the greater trans influence of the phosphorus ligand. In comparison, the sum of four angles around the palladium in complex **2**-$PdCl_2$ is 360.0-(1)°. The Pd−Cl(1) and Pd−Cl(2) bond lengths are 2.3127(12)

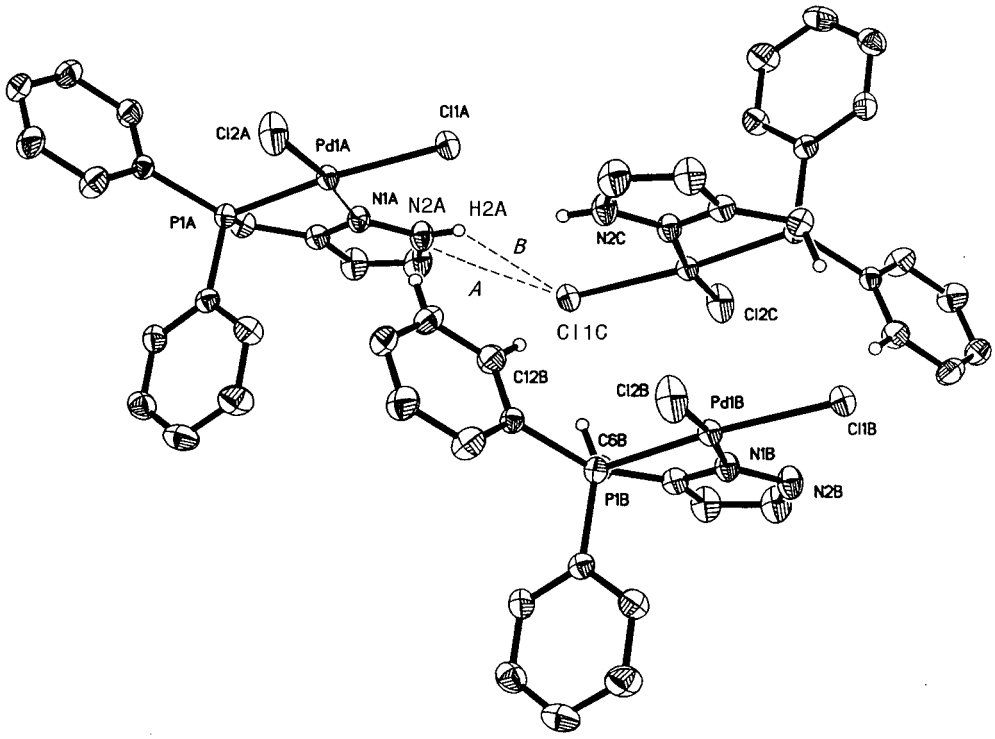


Figure 3. Diagram of part of the unit cell of **1**-$PdCl_2$, showing closest intermolecular contacts of chloride and the atoms of the nearest NH group. *A*: N2A−Cl1C = 3.280 Å. *B*: H2A−Cl1C = 2.587 Å.

Table 2. Selected Bond Lengths (Å) and Angles (deg) for Palladium Complexes **1**-$PdCl_2$, **2**-$PdCl_2$, **3**-$PdCl_2$, and **4**-$PdCl_2$

			3-$PdCl_2$		
bond lengths and angles	**1**-$PdCl_2$	**2**-$PdCl_2$	molecule 1	molecule 2	**4**-$PdCl_2$
Pd−N(1)	2.011(3)	1.987(4)	2.017(7)	2.024(7)	2.007(3)
Pd−Cl(1)	2.3941(10)	2.3127(12)	2.368(2)	2.363(3)	2.3078(9)
Pd−Cl(2)	2.2812(11)	2.2858(12)	2.276(2)	2.286(2)	2.2911(10)
Pd−L, L = P(1), S(1)	2.2097(10)	2.2716(12)	2.202(2)	2.205(2)	2.2661(9)
Cl(1)−H(2A)	2.796	2.738	na	na	na
Cl(1)−H intermolecular	2.587	2.772	na	na	na
N(1)−Pd−L, L = P(1), S(1)	81.10(10)	83.93(11)	85.1(2)	84.6(2)	85.02(8)
P(1)−Pd−Cl(2)	90.99(4)	91.28(5)	89.17(2)	89.49(9)	90.53(4)
N(1)−Pd−Cl(1)	91.86(10)	91.37(11)	92.8(2)	92.7(2)	91.31(8)
Cl(1)−Pd−Cl(2)	95.96(4)	93.42(5)	92.87(2)	93.21(11)	93.11(4)

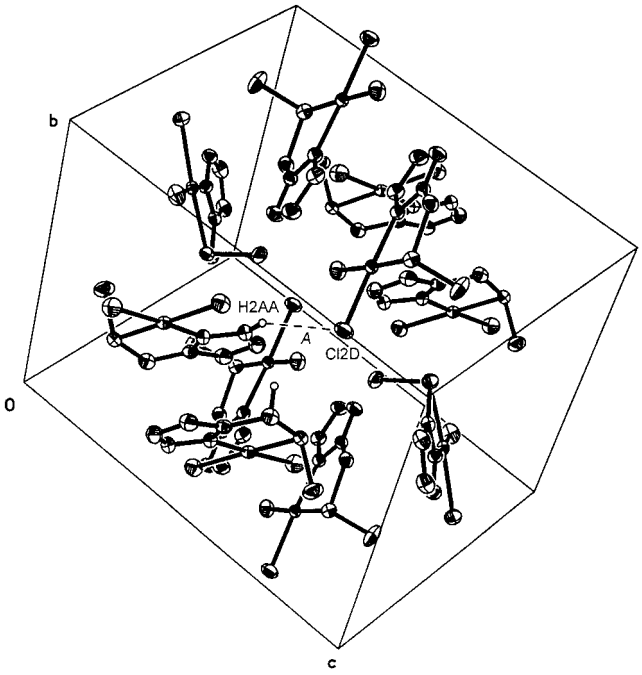
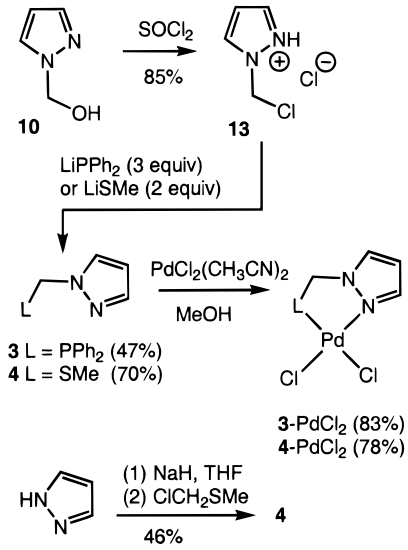


Figure 4. Diagram of the unit cell of **2**-$PdCl_2$, showing the closest intermolecular contacts of chloride and the atoms of the nearest NH group. *A*: H2AA−Cl2D = 2.772 Å.

and 2.2858(12) Å, respectively, which are quite consistent with the similar trans influence for nitrogen and sulfur. In the structure of **1**-$PdCl_2$, the intramolecular bond distance between Cl(1) and N−*H* hydrogen is 2.796 Å, but there is an even closer intermolecular contact between Cl(1) and an N−*H* hydrogen on another molecule in the unit cell (2.587 Å, see Figure 3). In thioether complex **2**-$PdCl_2$, the intramolecular bond distance between Cl(1) and N−H hydrogen is 2.738 Å (Figure 2), whereas the nearest intermolecular contact between Cl(1) and an N-*H* hydrogen on another molecule is 2.772 Å (Figure 4). Similar intramolecular[14] and intermolecular[14e,15] contacts between halide and pyrazole ligands have been invoked as proof of hydrogen bonding. For comparison, van der Waals radii of H and Cl are 1.20 and 1.75 Å, respectively,[16] consistent with identification of the hydrogen−chlorine contacts seen in structures of **1**-$PdCl_2$ and **2**-$PdCl_2$ as hydrogen bonds.

Scheme 3



Synthesis and Properties of 1-Substituted Pyrazole Ligands 3 and 4 and Their Complexes. The isoelectronic ligands **3** and **4** lacking an N−H functional group because of the attachment of the side chain at the 1-position on the pyrazole ring have been prepared in two steps from 1-hydroxymethylpyrazole (**10**). These ligands give access to complexes not capable of hydrogen bonding when chelated to a metal through phosphorus or sulfur and the unsubstituted nitrogen, and allow for a direct comparison with their N−H derivatives **1**-$PdCl_2$ and **2**-$PdCl_2$. The synthesis of chelating ligands **3** and **4** is outlined in Scheme 3. Literature methods were used to convert the alcohol functionality in **10** to a chloride in hydrochloride salt **13**.[17] Chloride **13** was then treated with lithium diphenylphosphide and lithium thiomethoxide in the same way as was isomer **12** to give either phosphine **3** or thioether **4** in 47% or 70% yield, respectively. Thioether **3** could also be prepared from the treatment of pyrazole with sodium hydride[18] and $ClCH_2SCH_3$ in 46% yield. The Ph_2PCH_2 side chain in ligand **3** could be identified by a singlet in the $^{31}P\{^1H\}$ NMR spectrum at −14.98 ppm, a doublet in the $^{13}C\{^1H\}$ NMR spectrum at 49.98 ppm, and a doublet in the ^1H NMR spectrum at 5.47 ppm for the methylene bridging unit. The $MeSCH_2$ side chain of **4** was identified by two singlets in the ^1H NMR spectrum at 2.12 and 5.15 ppm for the methyl and methylene protons, respectively.

Coordination of the $PdCl_2$ fragment to ligands **3** and **4** gave complexes **3**-$PdCl_2$ and **4**-$PdCl_2$ in 83% and 78% yields,

(14) Intramolecular hydrogen bonding between halide and pyrazole ligands: (a) Reedijk, J.; Stork-Blaisse, B. A.; Verschoor, G. C. *Inorg. Chem.* **1971**, *10*, 2594−2599. (b) Mighell, A. D.; Reimann, C. W.; Santoro, A. *Acta Crystallogr., Sect. B* **1969**, *B25*, 595−599. (c) Reimann, C. W. *J. Chem. Soc., Chem. Commun.* **1969**, 145−146. (d) Reimann, C. W.; Mighell, A. D.; Mauer, F. A. *Acta Crystallogr.* **1967**, *23*, 135−141. (e) Esteruelas, M. A.; Oliván, M.; Oñate, E.; Ruiz, N.; Tajada, M. A. *Organometallics* **1999**, *18*, 2953−2960.

(15) Intermolecular hydrogen bonding involving pyrazole ligands: (a) Reference 10a (to ionic chloride). (b) Reference 10f (Pd−Cl···H−N with H···Cl = 2.40 A). (c) For a related complex, see: Redmore, S. M.; Rickard, C. E. F.; Webb, S. J.; Wright, L. J. *Inorg. Chem.* **1997**, *36*, 4743−4748.

(16) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441−451.

(17) Katritzky, A. R.; Lam, J. N. *Can. J. Chem.* **1989**, *67*, 1144−1147.

(18) Begtrup, M.; Larsen, P. *Acta Chem. Scand.* **1990**, *44*, 1050−1057.

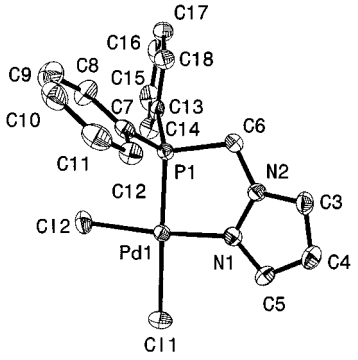


Figure 5. Molecular structure of **3**-$PdCl_2$.

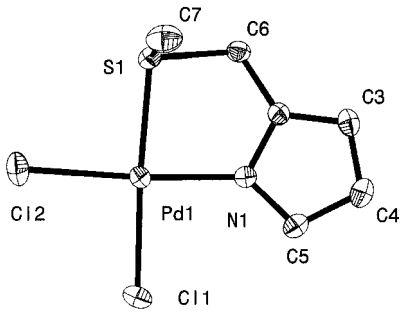


Figure 6. Molecular structure of **4**-$PdCl_2$.

respectively (Scheme 3), using the same conditions developed for their isomers. NMR spectral changes on complexation were similar to those seen in the reactions of **1** and **2**. Coordination of phosphorus to the metal in **3**-$PdCl_2$ was revealed by a significant downfield ^{31}P chemical shift (43.43 ppm). Binding of sulfur in **4**-$PdCl_2$ with the formation of a stereogenic center and a pair of diastereotopic protons at the methylene carbon was shown by the two mutually coupled doublets at 5.38 and 5.51 ppm ($J = 16.5$ Hz) in the ^1H NMR spectrum.

Crystals of the new Pd(II) complexes suitable for X-ray diffraction were grown by the slow evaporation of dichloromethane at room temperature (**3**-$PdCl_2$) or by diffusion of acetone into a solution of **4**-$PdCl_2$ and DMSO. The solid state structures of **3**-$PdCl_2$ and **4**-$PdCl_2$ were solved as described in Table 1, and the top ORTEP views of both complexes are shown in Figures 5 and 6.

The unit cell of **3**-$PdCl_2$ contains two independent molecules, whose metrical parameters are virtually the same, within experimental uncertainty. For simplicity only the bond lengths and angles for molecule 1 are described (Table 2). Complex **3**-$PdCl_2$ is a square planar complex with the sum of four angles around the palladium equal to 359.9(2)°. The large difference in the bond lengths Pd−Cl(1) [2.368(2) Å] and Pd−Cl(2) [2.276(2) Å] is ascribed to the stronger trans influence of the phosphorus. In contrast to the complexes with an N−H moiety, there are no apparent intermolecular interactions in the unit cell of **3**-$PdCl_2$ or **4**-$PdCl_2$.

The sum of the four angles around the palladium in **4**-$PdCl_2$ is 359.9(1)°. The Pd−Cl(1) and Pd−Cl(2) bond lengths are 2.3078(9) Å and 2.2911(10) Å, respectively, almost identical to the analogous bond lengths in complex **2**-$PdCl_2$. However, there are no intermolecular interactions between Cl(1) or Cl(2) and C−*H* hydrogens on other molecules, which is consistent with the absence of an N−H hydrogen bond donor. Selected bond lengths and angles are shown in Table 2.

Comparing isomeric complexes (**1**-$PdCl_2$ vs **3**-$PdCl_2$, **2**-$PdCl_2$ vs **4**-$PdCl_2$), the Pd−ligand distances are within 0.03 Å. As for interligand bond angles, complexes **1**-$PdCl_2$ and **2**-$PdCl_2$ have N−Pd−L and Cl(1)−Pd−Cl(2) angles smaller than do **3**-$PdCl_2$ and **4**-$PdCl_2$, respectively. These more acute bond angles may be attributed to different five-membered rings in complexes **1**-$PdCl_2$ and **2**-$PdCl_2$ (P/S, C, C, N, Pd) vs the five-membered rings in **3**-$PdCl_2$ and **4**-$PdCl_2$ (P/S, C, N, N, Pd) and not due to a chemical difference from the direct coordination of the ligands on palladium.

Conclusion

Four new ligands designed to form bidentate complexes using a soft donor atom and a pyrazole nitrogen have been synthesized and their corresponding *cis*-dichloropalladium(II) complexes prepared. In the solid state, the two palladium complexes (**1**-$PdCl_2$ and **2**-$PdCl_2$) with a pyrazole N−H group show intra- and intermolecular hydrogen bonding to the chloride ligands. The intramolecular distances between chloride and the NH proton are comparable to the closest intermolecular contacts found in the solid state structures. In contrast, isomeric complexes lacking an N−H group (**3**-$PdCl_2$ and **4**-$PdCl_2$) show no hydrogen bonding. Future work will explore the cooperativity of the metal center and the coordinated pyrazole ligand.

Acknowledgment. NSF funding (CHE 9413802) for a 500 MHz NMR spectrometer for SDSU and CONACYT Proyecto Infraestructura funding (F264-E9207) for an X-ray diffractometer are gratefully acknowledged.

Supporting Information Available: Tables of all crystal bond distances and angles, anisotropic displacement coefficients, H atom coordinates, and anisotropic displacement coefficients and diagrams of intermolecular contacts for **1**-$PdCl_2$ and **2**-$PdCl_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

IC990995Q