Convenient Synthesis of α-Chiral Platinum Alkyls

Paola Bergamini,* Emiliana Costa, and Silvana Sostero

Dipartimento di Chimica dell'Università di Ferrara e Centro di Fotochimica CNR,
Via L. Borsari 46, 44100 Ferrara, Italy

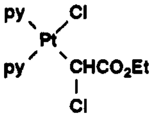
A. Guy Orpen and Paul G. Pringle*

School of Chemistry, University of Bristol, Cantocks Close, Bristol BS8 1TS, U.K.

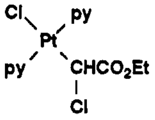
Received February 22, 1991

Summary: The platinum complexes [$PtX_2(\eta^2$-dppm)] (X = Cl, Br, I) and [$PtCl_2L_2$] (L_2 = dppe, 2 PPh_3, 1,5-cod) react with EtO_2CCHN_2 to give the racemic monoalkyl complexes [$PtX(CHXCO_2Et)L_2$] in high yield. Addition of EtO_2CCHN_2 to [$PtCl_2$\{(–)-diop\}] gives a 3:1 mixture of diastereoisomers of [$PtCl(CHClCO_2Et)$\{(–)-diop\}] from which the major isomer is readily separated and crystallized; the X-ray crystal structure reveals that the major isomer has the *R* configuration at the α-carbon atom.

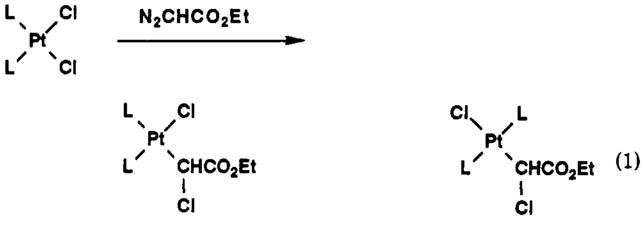
Transition-metal alkyls which are chiral at the α-carbon atom are invaluable for fundamental mechanistic studies[1] (e.g. oxidative additions, reductive eliminations, and insertions) and are purported intermediates in many asymmetric catalyses[2] (e.g. HX (X = H, HCO, CN, SiR_3, CH=CHR) additions to alkenes, Grignard cross-coupling reactions, alkene isomerizations). The most common way to synthesize α-chiral metal alkyls is by oxidative addition of a chiral haloalkane to a low-valent metal complex,[3] but because these syntheses are dependent on the availability of suitable chiral haloalkanes and require the oxidative addition to be highly stereospecific, they are of limited generality. We now report a simple, efficient, general route to highly functionalized, optically stable α-chiral platinum alkyls from readily available starting materials.



1a



2a



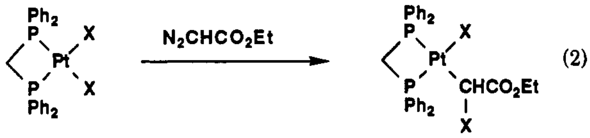
1b L = PPh_3

1c L_2 = 1,5-cyclooctadiene

1d L_2 = $Ph_2CH_2CH_2PPh_2$

1e L_2 = $Ph_2CH_2PPh_2$

2b L = PPh_3



1e X = Cl

1f X = Br

1g X = I

Jennings et al.[4] reported the synthesis of the cis/trans mixture of racemic complexes [$PtCl(CHClCO_2Et)py_2$] (**1a**, **2a**) by the reaction of ethyl diazoacetate with Zeise's dimer in the presence of pyridine. We have found that this route can be generalized to the synthesis of **1b–g** and **2b** by the reaction of ethyl diazoacetate with haloplatinum complexes of the type [$PtCl_2L_2$], where L_2 = 2 PPh_3, 1,5-cod, dppe, and dppm, and [$PtX_2(\eta^2$-dppm)], where X = Cl, Br, and I (see eqs 1 and 2).[5,6] For example, when [$PtCl_2(\eta^2$-dppm)] is treated with an excess of EtO_2CCHN_2, the monoalkyl complex [$PtCl(CHClCO_2Et)(\eta^2$-dppm)] (**1e**), which has been fully characterized,[7a] is the only product observed by $^{31}P\{^1H\}$ NMR spectroscopy. The ^1H NMR spectrum of **1e** reveals the inequivalence of the diastereotopic CH_2 protons

---

(1) Flood, T. C. *Topics in Inorganic and Organometallic Stereochemistry*; Wiley: New York, 1981.

(2) (a) Kagan, H. B. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Eds.; Pergamon: Oxford, U.K., 1982; Vol. 8, p 463. (b) Reference 1 in: Chu, K.-H.; Foxman, B. M.; Rosenblum, M.; Zhu, X.-Y. *Organometallics* **1990**, *9*, 3010.

(3) (a) Stille, J. K. In *The Chemistry of the Metal-Carbon Bond*; Hartley, F. R., Patai, S., Eds.; Wiley: New York, 1985; Vol. 2, p 625. (b) Becker, Y.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 838.

(4) Hanks, T. W.; Ekeland, R. A.; Emerson, K.; Larsen, R. D.; Jennings, P. W. *Organometallics* **1987**, *6*, 28.

(5) The analogous reaction of CH_2N_2 with complexes **1b–g** to give bis-insertion products [$Pt(CH_2X)_2L_2$] has been previously investigated by us and McCrindle et al.: (a) Alcock, N. W.; Pringle, P. G.; Bergamini, P.; Sostero, S.; Traverso, O. *J. Chem. Soc., Dalton Trans.* **1990**, 1553. (b) McCrindle, R.; Arsenault, G. J.; Farwaha, R. *J. Organomet. Chem.* **1985**, *236*, C51. (c) McCrindle, R.; Arsenault, G. J.; Farwaha, R.; Hampden-Smith, M. J.; Rice, R. E.; McLees, A. C. *J. Chem. Soc., Dalton Trans.* **1988**, 1773. (d) McCrindle, R.; Ferguson, G.; Arsenault, G. J.; McAlees, A. J.; Ruhl, B. L.; Sneddon, D. W. *Organometallics* **1986**, *5*, 1171.

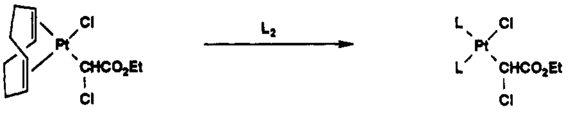
(6) Complexes **1b–e**, **2b**, **3a,b**, and **4a,b** can be made by two methods (eqs 1 and 3), exemplified here by the preparations of **3a,b** and **1e**: (a) In a typical reaction, 0.76 g (0.10 mmol) of [$PtCl_2$\{(–)-diop\}] was dissolved in 20 mL of dichloromethane and an excess of $N_2CHCOOEt$ (0.80 mmol) was added. After the mixture was stirred for 48 h, the solvent was removed under reduced pressure and the residue triturated with Et_2O to give a 3:1 mixture of products **3a,b** in 72% yield. Recrystallization from CH_2Cl_2/Et_2O gave pure **3a**. (b) In a typical reaction, 0.46 g (0.11 mmol) of [$PtCl(CHClCO_2Et)$(1,5-cod)] (**1c**) was dissolved in 5 mL of dichloromethane and then 0.042 g (0.11 mmol) of the dppm in 5 mL of CH_2Cl_2 was added dropwise over 10 min. After a further 30 min of stirring at room temperature, the solvent and the displaced 1,5-cod were removed under reduced pressure to give the crude product **1e**, which was recrystallized from CH_2Cl_2 and Et_2O in ca. 80% yield.

(7) (a) Characterization data for **1e**: Anal. Found (calcd for $C_{29}H_{28}Cl_2O_2P_5Pt$): C, 47.54 (47.32); H, 4.03 (3.83). Spectroscopic data for **1e**: IR (CsI pellet) ν(CO) 1720 (s), ν(PtCl) 290 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.02 (t, $^3J_{H-H}$ = 7.0 Hz, 3 H, CH_2CH_3), 3.30 (dq, $^3J_{H-H}$ = 7.0 Hz, $^2J_{H-H}$ = 11.25 Hz, 1 H, $CHCH_3$), 3.65 (dq, $^3J_{H-H}$ = 7.0 Hz, $^2J_{H-H}$ = 11.25 Hz, $CHCH_3$), 4.20 (m, 1 H, $CHPPh_2$), 4.35 (m, 1 H, $CHPPh_2$), 4.75 (d, J_{P-H} = 9.3 Hz, $^2J_{Pt-H}$ = 97.4 Hz, 1 H, CHClCOOEt); ^{31}P NMR ($CDCl_3$, 36.4 MHz) δ –47.7 (d, $^2J_{P-P}$ = 56 Hz, $^1J_{Pt-P}$ = 3485 Hz), –49.8 (d, $^2J_{P-P}$ = 56 Hz, $^1J_{Pt-P}$ = 1645 Hz). (b) Characterization data for **3a,b**: Anal. Found (calcd for $C_{35}H_{37}Cl_2O_2P_2Pt$ with 0.25 mol of CH_2Cl_2): C, 47.91 (48.00); H, 4.31 (4.41). Spectroscopic data for **3a,b**: IR (CsI pellet) ν(CO) 1730 (s), ν(PtCl) 300 (m) cm^{-1}. ^{31}P NMR ($CDCl_3$, 36.4 MHz): **3a** δ 1.51 (d, $^2J_{P-P}$ = 20 Hz, $^1J_{Pt-P}$ = 4099 Hz), –0.5 (d, $^2J_{P-P}$ = 20 Hz, $^1J_{Pt-P}$ = 1946 Hz); **3b**, δ 1.51 (d, $^2J_{P-P}$ = 20 Hz, $^1J_{Pt-P}$ = 4099 Hz), –1.3 (d, $^2J_{P-P}$ = 20 Hz, $^1J_{Pt-P}$ = 1932 Hz). ^1H NMR ($CDCl_3$, 300 MHz): pure **3a**, δ 1.03 (s, 3 H, $CH_3CMe(O)_2$), 1.21 (s, 3 H, $CH_3CMe(O)_2$), 1.22 (t, $^3J_{H-H}$ = 10.8 Hz, 3 H, CH_2CH_3), 2.24, 2.60, 2.98, 3.47 (4 multiplets, each 1 H, PCH), 3.73 (m, 1 H, $CHCH_3$), 3.78 (m, 1 H, $CHCH_3$), 4.0–4.2 (complex m, 3 H, $OCH(CH_2)CH(CH_2OCMe_2$ overlapping with $CHCO_2Et$). The data for the other complexes reported here are deposited in the supplementary material.

0276-7333/91/2310-2989$02.50/0

in the dppm backbone, consistent with the presence of the α-chiral center.

The complex [PtCl(CHClCO$_2$Et)(1,5-cod)] (**1c**) is a convenient starting material for the synthesis of other [PtCl(L)$_2$(CHClCO$_2$Et)] species by substitution of 1,5-cod (eq 3).[6b] When **1c** is treated with the chiral diphosphine



(3)

1c

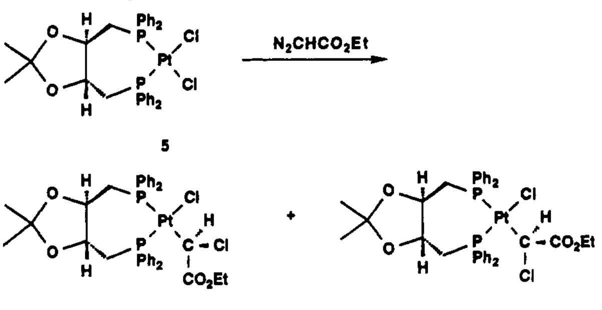
1d L$_2$ = Ph$_2$CH$_2$CH$_2$PPh$_2$

1e L$_2$ = Ph$_2$CH$_2$PPh$_2$

3a,b L$_2$ = (-)-diop

4a,b L$_2$ = (+)-chiraphos

(−)-diop or (+)-chiraphos, the products, as shown by ^{31}P{^{1}H} NMR spectroscopy, are 1:1 mixtures of diastereoisomers **3a,b** or **4a,b**. Significantly, treatment of [PtCl$_2${(−)-diop}] (**5**) with EtO$_2$CCHN$_2$ gave the same diastereoisomers[7b] in solution (eq 4), but in the ratio ca. 3:1. The major isomer



5

(4)

3a **3b**

3a was readily separated by fractional crystallization from CH$_2$Cl$_2$/diethyl ether; CDCl$_3$ solutions of the pure **3a** were found to be optically stable at +20 °C for at least 14 days.

The X-ray crystal structure[8] of the major isomer **3a** as its dichloromethane solvate was determined and reveals that the configuration at the α-carbon is *R* (see Figure 1). The chiraphos complex [PtCl$_2${(*R*,*R*)-Ph$_2$PCHMeCHMePPh$_2$}] reacts similarly with EtO$_2$CCHN$_2$ to give **4a,b** in a similar ratio (ca. 3:1), but assignment of *R* or *S* configuration has not been proven.

The diastereoselective insertion reaction shown in eq 4 is a simple, general,[9] and efficient method for the synthesis of chiral platinum alkyls which we are presently developing by extending the reaction to other metals (e.g. Pd, Rh, Ni, Cu), to other diazoalkanes, and by elaboration of the chemistry of the ester and halogen functionalities.[10] It is well-known that many late-transition-metal complexes catalyze carbene-like reactivity of diazoacetates[11] such as alkane C–H insertion,[12] dimerization to give RO$_2$CCH=CHCO$_2$R,[13] ylide formation,[14] and most importantly asymmetric cyclopropanation.[15] The accepted mechanism for this disparate group of reactions involves discrete metal carbene intermediates.[16] Since in many cases the catalysts used are halometal complexes,[13–16] our results suggest that α-haloalkyl complexes may be involved, and this possibility is under investigation.

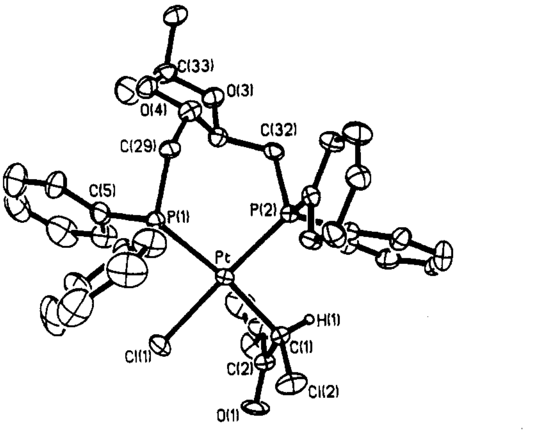


Figure 1. Molecular structure of **3a** showing atom labeling. Important molecular dimensions include the following: bond lengths (Å) Pt–C(1) = 2.114 (13), Pt–P(1) = 2.320 (3), Pt–P(2) = 2.233 (3), Pt–Cl(1) = 2.362 (3); bond angle (deg) P(2)–Pt(2)–P(1) = 96.3 (1); torsion angle (deg) P(2)–Pt–C(1)–H(1) = 5 (10).

Acknowledgment. We thank NATO for the provision of a travel grant and Johnson-Matthey for a generous loan of platinum salts.

Supplementary Material Available: Text describing syntheses and spectroscopic characterizations of complexes **1b–g**, tables of microanalytical data for **1b–g**, **3a,b**, and **4a,b**, and listings of atomic coordinates, bond lengths and angles, and anisotropic displacement parameters for **3a**·CH$_2$Cl$_2$ (10 pages); a listing of observed and calculated structure factors for **3a**·CH$_2$Cl$_2$ (13 pages). Ordering information is given on any current masthead page.

---

(8) Crystal data for **3a**·CH$_2$Cl$_2$: C$_{36}$H$_{39}$Cl$_4$P$_2$Pt, M_r = 870.6, monoclinic, space group $P2_1$ (No. 4), a = 9.775 (2) Å, b = 15.964 (2) Å, c = 12.376 (3) Å, β = 91.31 (2)°, V = 1930.8 (7) Å^3, Z = 2, D_{exptl} = 1.50 g cm^{-3}, λ = 0.71069 Å, μ(Mo K$_\alpha$) = 40.7 cm^{-1}, F(000) = 926, T = 293 K. Full-matrix least-squares refinement (427 parameters) converged to final residual indices R = 0.038, R_w = 0.047, and S = 1.35 with use of 3277 absorption-corrected data for which $I > 2\sigma(I)$. The absolute structure shown in Figure 1 was confirmed by refinement.

(9) Preliminary ^{31}P{^{1}H} NMR experiments have shown that [PtI$_2$(diop)] and complexes of other chiral diphosphines (e.g. [PtCl$_2${(*S*,*S*)-Ph$_2$PCHMeCH$_2$CHMePPh$_2$}]) react diastereoselectively with EtO$_2$CHN$_2$.

(10) The reactivity and utility of chloroalkyl transition-metal complexes have recently been studied by several groups: (a) Huser, M.; Youinou, M.-T.; Osborn, J. A. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1386. (b) Marder, T. B.; Fultz, W. C.; Calabrese, J. C.; Harlow, R. L.; Milstein, D. *J. Chem. Soc., Chem. Commun.* **1987**, 1543. (c) Werner, H.; Hofmann, L.; Paul, W.; Schubert, U. *Organometallics* **1988**, *7*, 1106. (d) Hubbard, J. L.; McVicar, W. K. *J. Am. Chem. Soc.* **1986**, *108*, 6422. (e) Hubbard, J. L.; McVicar, W. K. *Organometallics* **1990**, *9*, 2683. (f) McCrindle, R.; Arsenault, G. J.; Farwaha, R.; Hampden-Smith, M. J.; McLees, A. J. *J. Chem. Soc., Chem. Commun.* **1986**, 943. (g) McCrindle, R.; Arsenault, G. J.; Farwaha, R.; McAlees, A. J.; Sneddon, D. W. *J. Chem. Soc., Dalton Trans.* **1989**, 761. (h) McCrindle, R.; Ferguson, G.; McAlees, A. J. *J. Chem. Soc., Chem. Commun.* **1990**, 1524.

(11) Adams, J.; Spero, D. M. *Tetrahedron* **1991**, *47*, 1765.

(12) Demonceau, A.; Noels, A. F.; Hubert, A. J.; Teyssie, P. *J. Chem. Soc., Chem. Commun.* **1981**, 688.

(13) (a) Armstrong, K. R. *J. Org. Chem.* **1966**, *31*, 618. (b) Werner, H.; Richards, J. H. *J. Am. Chem. Soc.* **1968**, *90*, 4976.

(14) (a) Kirmse, W.; Kapps, M. *Chem. Ber.* **1968**, *101*, 994. (b) Ando, W.; Kondo, S.; Nakayama, K.; Ichibori, K.; Koshoda, H.; Yamamoto, H.; Imai, I.; Nakaido, S.; Migita, T. *J. Am. Chem. Soc.* **1972**, *94*, 3870. (c) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* **1981**, *46*, 5094.

(15) (a) Tatsuno, Y.; Konishi, A.; Nakamura, A.; Otsuka, S. *J. Chem. Soc., Chem. Commun.* **1974**, 588. (b) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1977**, 2599. (c) Nakamura, A.; Koyama, T.; Otsuka, S. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 593. (d) Nakamura, A.; Konishi, A.; Tatsuno, Y.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, 100, 3443. (e) Nakamura, A.; Konishi, A.; Tsujitani, R.; Kudo, M.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3449. (f) Nakamura, A. *Pure Appl. Chem.* **1978**, *50*, 37. (g) Melnick, M. J.; Bisaha, S. N.; Gammill, R. B. *Tetrahedron Lett.* **1990**, *31*, 961. (h) Doyle, M. P.; Brandes, B. D.; Kazala, A. P.; Pieters, R. J.; Jarstfer, M. B.; Watkins, L. M.; Eagle, C. T. *Tetrahedron Lett.* **1990**, *31*, 6613. (i) Doyle, M. P.; Bagheri, V.; Wandless, T. J.; Harn, N. K.; Brinker, D. A.; Eagle, C. T.; Loh, K.-L. *J. Am. Chem. Soc.* **1990**, *112*, 1906. (j) Doyle, M. P.; Pieters, R. J.; Martin, S. F.; Austin, R. E.; Oalmann, C. J.; Muller, P. *J. Am. Chem. Soc.* **1991**, *113*, 1423. (k) Anciaux, A. J.; Hubert, A. J.; Noels, A. F.; Petiniot, N.; Teyssie, P. *J. Org. Chem.* **1980**, *45*, 695. (l) Hubert, A. J.; Noels, A. F.; Anciaux, A. J.; Teyssie, P. *Synthesis* **1976**, 600. (m) European Patent No. 22608 (1981) to ICI; *Chem. Abstr.* **1981**, *95*, 114886.

(16) (a) Moser, W. R. *J. Am. Chem. Soc.* **1969**, *91*, 1135. (b) Moser, W. R. *J. Am. Chem. Soc.* **1969**, *91*, 1141. (c) Moritani, I.; Yamamoto, Y.; Konoshi, H. *J. Chem. Soc. D* **1969**, 1457. (d) Bien, S.; Gillon, A.; Kohen, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 489. (e) Doyle, M. P.; Dorow, R. L.; Buhro, W. E.; Griffin, J. H.; Tamblyn, W. H.; Trudell, M. L. *Organometallics* **1984**, *3*, 44. (f) Brookhart, M.; Studabaker, W. B. *Chem. Rev.* **1987**, *87*, 411. (g) Brookhart, M.; Liu, Y.; Goldman, E. W.; Timmers, D. A.; Williams, G. D. *J. Am. Chem. Soc.* **1991**, *113*, 927.