Diastereoselective C–C Bond Formation by Carbene Insertions into Pt–CH$_3$ Bonds

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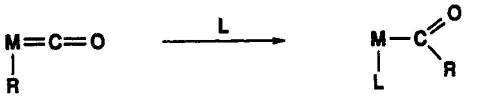
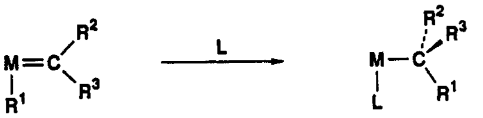
Summary: The platinum complexes [PtX(CH$_3$)(*S,S*-diop)] *(X = Cl, Br, I) react quantitatively with* N$_2$CHCO$_2$R *(R = Et, R-menthyl) in polar solvents* (CD$_3$CN, DMSO) *to give* [PtX{CH(CH$_3$)CO$_2$R}(*S,S*-diop)] *as a 2:1 (R = Et) or 4:1 (R = R-menthyl) mixture of diastereomers. The major diastereomer when X = Cl and R = Et is readily separated, and its crystal structure reveals that the configuration about the α-carbon is R; this complex is configurationally stable in solution for at least 12 days. In less polar solvents* (CDCl$_3$, C$_6$D$_6$)*, reaction of* N$_2$CHCO$_2$Et *with* [PtX(CH$_3$)(*S,S*-diop)] *(X = Br, I) give the products of carbene insertion into the Pt–X as well as Pt–C bonds.*

A classical method for creating a new C–C bond within the coordination sphere of a metal is the ubiquitous carbonyl insertion reaction (eq 1), which involves the migration of an alkyl ligand to a coordinated CO to give a metal acyl.[1] Though a less well-studied reaction, the related migration of an alkyl ligand to a coordinated carbene to give a new metal alkyl (eq 2) has attracted considerable attention recently.[2] One important feature is that when R^1 ≠ R^2 ≠ R^3, a new chiral center is formed, and if the stereochemistry at the α-carbon could be controlled, the potential for application of this reaction in synthesis would be greatly increased. It was therefore of interest to investigate whether diastereoselective carbene insertions into Pt–C bonds were possible. In this paper we report that diazo esters react with [PtX(CH$_3$)(diop)] (diop = 2,3-isopropylidene-2,3-*trans*-dihydroxy-1,4-bis(diphenylphosphino)butane) diastereoselectively to give either Pt–C or Pt–X insertion products, depending on the reaction conditions.



(1)



(2)

When [PtCl(CH$_3$)(*S,S*-diop)] (**1a**) is treated[3] with 1 equiv or an excess of N$_2$CHCO$_2$Et in CH$_2$Cl$_2$, nitrogen is evolved and two products in the ratio of 2:1 are observed by ^{31}P NMR spectroscopy. They have been assigned the diastereoisomeric structures **2a** and **3a** on the basis of a combination of elemental analysis and NMR spectroscopy (eq 3).[4a] The major isomer readily crystallized from a CH$_2$Cl$_2$/Et$_2$O solution, and its X-ray crystal structure[5] (see Figure 1) revealed that the absolute configuration at the α-carbon is *R*. No epimerization or decomposition was observed when a solution of pure **2a** in CD$_2$Cl$_2$ was left to stand for 12 days, despite the presence of β-hydrogens.[6]

In an attempt to improve the diastereoselectivity of the Pt–C insertion, **1a** was treated with the bulky, chiral diazo ester N$_2$CHCO$_2$(*R*-menthyl), and indeed the ratio of

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[1] For leading references see: (a) Collman, J. P.; Hegadus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987. (b) Bock, P. L.; Boschetto, D. J.; Ramussen, J. R.; Dimers, J. P.; Whitesides, G. M. *J. Am. Chem. Soc.* 1974, *96*, 2814. (c) Anderson, G. K.; Cross, R. J. *Acc. Chem. Res.* 1984, 67. (d) Dekker, G. P. C. M.; Elsevier, C. J.; Vrieze, K.; van Leeuwen, P. W. N. M.; *Organometallics* 1992, *11*, 1598.

[2] For leading references see: (a) Hoover, J. F.; Stryker, J. M. *J. Am. Chem. Soc.* 1990, *112*, 464. (b) Trace, R. L.; Sanchez, J.; Yang, J.; Yin, J.; Jones, W. M. *Organometallics* 1992, *11*, 1440. (c) Adams, H.; Bailey, N. A.; Bentley, G. W.; Tattershall, C. E.; Taylor, B. F.; Winter, M. J. *J. Chem. Soc., Chem. Commun.* 1992, 533.

[3] In a typical reaction, 0.20 g (0.27 mmol) of [PtCl(CH$_3$)(*S,S*-diop)] was dissolved in 8 mL of CH$_2$Cl$_2$ and 1.40 mL of a 0.44 M CH$_2$Cl$_2$ solution of N$_2$CHCO$_2$Et (0.62 mmol) was added dropwise over 5 min and the mixture stirred for 16 h under N$_2$. The solution was evaporated to 0.5 mL and then 15 mL of *n*-pentane added to precipitate the white solid product, a 2:1 mixture of **2a** and **3a** (0.182 g, 82%). Pure **2a** was obtained by recrystallization from CH$_2$Cl$_2$/Et$_2$O. Details of the preparation of all other complexes reported here are given in the supplementary material.

[4] (a) Characterization data for **2a** and **3a** are as follows. Anal. Found (calcd) for C$_{36}$H$_{41}$ClO$_4$P$_2$Pt·CH$_2$Cl$_2$: C, 48.66 (48.56); H, 4.81 (4.74). IR (CsCl pellet): ν(CO) 1701 (s), ν(PtCl) 290 (m) cm^{-1}. Selected NMR data for **2a**: ^{1}H NMR (CDCl$_3$, 300 MHz) δ 0.66 ($^3J_{\mathrm{Pt-H}}$ = 32.6 Hz, $^3J_{\mathrm{H-H}}$ = 7.7 Hz, $^4J_{\mathrm{P-H}}$ = 7.7 Hz, 3H, PtCHCH_3), 2.15 (assigned from COSY to PtCHCH$_3$); ^{31}P NMR (CDCl$_3$, 81 MHz) δ 5.6 (d, $^2J_{\mathrm{P-P}}$ = 15 Hz, $^1J_{\mathrm{Pt-P}}$ = 4305 Hz), 5.1 (d, $^2J_{\mathrm{P-P}}$ = 15 Hz, $^1J_{\mathrm{Pt-P}}$ = 1807 Hz); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 15.3 ($^2J_{\mathrm{Pt-C}}$ = 57.6 Hz, PtCHCH$_3$), 32.0 (assigned from DEPT to PtCHCH$_3$). Selected NMR data for **3a**: ^{1}H NMR (CDCl$_3$, 300 MHz) δ 0.9 ($^3J_{\mathrm{Pt-H}}$ not resolved, $^3J_{\mathrm{H-H}}$ = 7.5 Hz, $^4J_{\mathrm{P-H}}$ = 7.5 Hz, 3H, PtCHCH_3); ^{31}P NMR (CDCl$_3$, 81 MHz) δ 2.8 (d, $^2J_{\mathrm{P-P}}$ = 17 Hz, $^1J_{\mathrm{Pt-P}}$ = 4296 Hz), 3.3 (d, $^2J_{\mathrm{P-P}}$ = 17 Hz, $^1J_{\mathrm{Pt-P}}$ = 1769 Hz). (b) Characterization data for **8c** and **9c** are as follows. Anal. Found (calcd) for C$_{36}$H$_{41}$IO$_4$P$_2$Pt·CH$_2$Cl$_2$: C, 44.14 (44.15); H, 4.37 (4.31). IR (CsCl pellet): ν(CO) 1709 (s) cm^{-1}. Selected NMR data: ^{1}H NMR (CDCl$_3$, 300 MHz) δ 0.50 ($^2J_{\mathrm{Pt-H}}$ = 63.3 Hz, $^3J_{\mathrm{P-H}}$ = 7.1 Hz, 3H, PtCH_3), signals for minor isomer not observed; ^{31}P NMR (CDCl$_3$, 81 MHz) major isomer δ 9.5 (d, $^2J_{\mathrm{P-P}}$ = 11 Hz, $^1J_{\mathrm{Pt-P}}$ = 2483 Hz), 7.4 (d, $^2J_{\mathrm{P-P}}$ = 11 Hz, $^1J_{\mathrm{Pt-P}}$ = 1801 Hz), minor isomer δ 8.5 (d, $^2J_{\mathrm{P-P}}$ = 11 Hz, $^1J_{\mathrm{Pt-P}}$ = 2461 Hz), 7.8 (d, $^2J_{\mathrm{P-P}}$ = 11 Hz, $^1J_{\mathrm{Pt-P}}$ = 1783 Hz); ^{13}C NMR (CDCl$_3$, 75 MHz) δ 15.0 (PtCHI, assigned from DEPT), 8.5 ($^1J_{\mathrm{Pt-C}}$ = 551 Hz, $J_{\mathrm{P-C}}$ = 87.2, 8.8 Hz, PtCH$_3$), signals for the minor isomer not observed; ^{195}Pt NMR (CDCl$_3$, 85.6 MHz) major isomer, δ −205 ($^1J_{\mathrm{Pt-P}}$ = 1804, 2489), minor isomer δ −199 ($^1J_{\mathrm{Pt-P}}$ = 1778, 2462 Hz). The data for the other complexes reported here are deposited in the supplementary material.

[5] Crystal data for **2a**: C$_{36}$H$_{41}$ClO$_4$P$_2$Pt, M_r = 830.2, orthorhombic, space group $P2_12_12$ (No. 18), a = 16.520(5) Å, b = 20.722(6) Å, c = 10.535(4) Å, V = 3607(2) Å^3, Z = 4, D_{calc} = 1.53 g cm^{-3}, $\bar{\lambda}$ = 0.710 73 Å, μ(Mo Kα) = 40.9 cm^{-1}, $F(000)$ = 1656, T = 293 K. Full-matrix least-squares refinement (398 parameters) converged to final residual indices R = 0.047, R_w = 0.054, and S = 1.34 using 2802 absorption-corrected data for which $I > 2\sigma(I)$. The absolute structure shown in Figure 1 was confirmed by refinement.

[6] It has been suggested that species containing the MCH(CH$_3$)CO$_2$Et group would be expected to epimerize via a β-hydrogen-elimination mechanism; see: Flood, T. C. *Topics in Inorganic and Organometallic Stereochemistry*; Wiley: New York, 1981; p 37.

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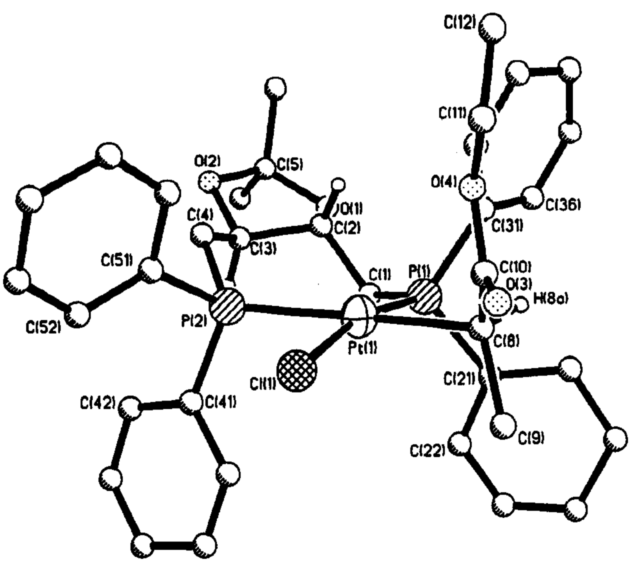
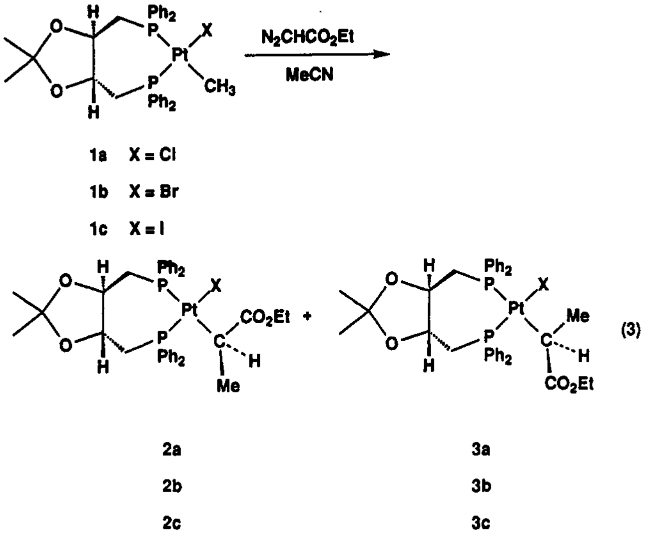
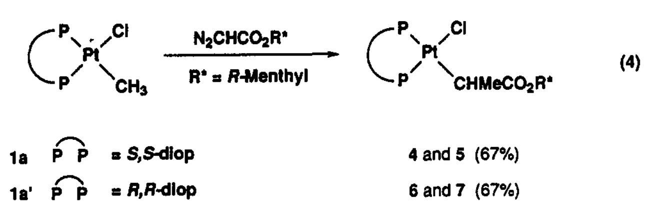


Figure 1. Molecular structure of **2a**, showing the atom labeling. Important molecular dimensions include the following: bond lengths (Å) Pt–C(8) = 2.171(14), Pt–P(1) = 2.227(4), Pt–P(2) = 2.331(4), Pt–Cl(1) = 2.364(4); bond angle (deg) P(1)–Pt(1)–P(2) = 100.1(1)°; torsion angle (deg) P(1)–Pt–C(8)–H(8a) = 16.5°.

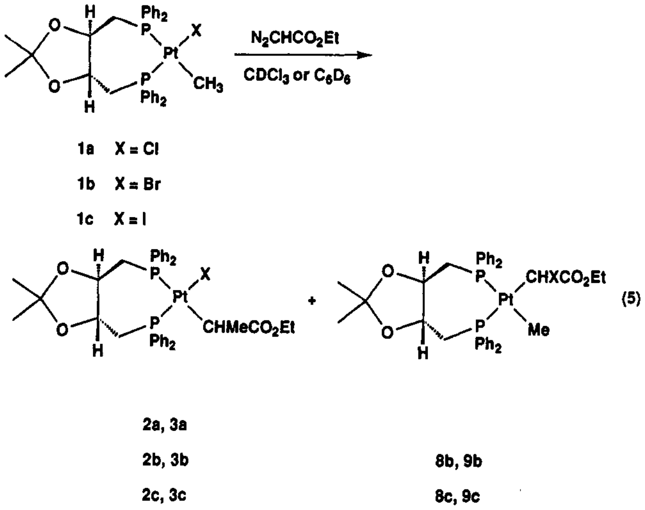


diastereoisomers **4** and **5** was significantly greater at 4:1. However, this is not simply an effect of the bulk of the ester, since treatment of the enantiomer [PtCl(CH_3)(*R,R*-diop)] (**1a′**) with N_2CHCO_2(*R*-menthyl) gave only a 2:1 ratio of diastereoisomers **6** and **7**, and it thus appears that some double asymmetric induction by the menthyl diazoacetate is involved.[7] The absolute configurations at the α-carbons in these menthyl products (eq 4) have not been determined.



The chloride ligands in **2a** and **3a** are readily substituted by bromide or iodide by metathesis with NaBr or NaI in acetone, and the ratios of the bromo (**2b, 3b**) and iodo (**2c, 3c**) products are the same as in the chloride precursors. The iodo species **2c** and **3c** are labile in solution, significant decomposition occurring even under the mild conditions of the metathesis.

The species **2b,c** and **3b,c** are also observed (2:1 ratio again) as the products of Pt–C insertion when [PtX(CH_3)(S,S-diop)] (X = Br (**1b**), I (**1c**)) is treated with N_2CHCO_2Et in CH_3CN (eq 3). However, when less polar solvents are used for these reactions (e.g. $CDCl_3$), in addition to **2b,c** and **3b,c** a second group of products are formed which are assigned diastereomeric structures **8b,c** and **9b,c**, i.e. the products of Pt–X insertion (eq 5).[8] The proportion of Pt–C to Pt–X insertion is a function of (a) the solvent, as DMSO and MeCN favor Pt–C insertion and $CDCl_3$ and benzene favor Pt–X insertion, and (b) the halogen, as treatment of [PtX(CH_3)(*S,S*-diop)] with N_2CHCO_2Et in $CDCl_3$ gave 100%, 80%, and 55% Pt–C insertion products for X = Cl, Br, and I, respectively. By using benzene as the reaction medium, **8c** and **9c** have been isolated (62% yield) and characterized.[4b]



The Pt–I insertion products **8c** and **9c** are not intermediates in the formation of the Pt–C insertion products **2c** and **3c**, since isolated samples of **8c** and **9c** dissolved in MeCN show no tendency to spontaneously isomerize to **2c** and **3c** over a period of 3 days. Hence, the Pt–I and Pt–C insertions occur by independent pathways. A mechanism consistent with our observations is shown in Scheme 1, which depicts displacement of halogen to give the alkyl carbene species **A**, within which C–C bond formation takes place by methyl migration,[9] probably solvent assisted. When the cationic intermediate **A** is invoked, the following observations can be rationalized: (i) polar, coordinating solvents promote Pt–C insertion;

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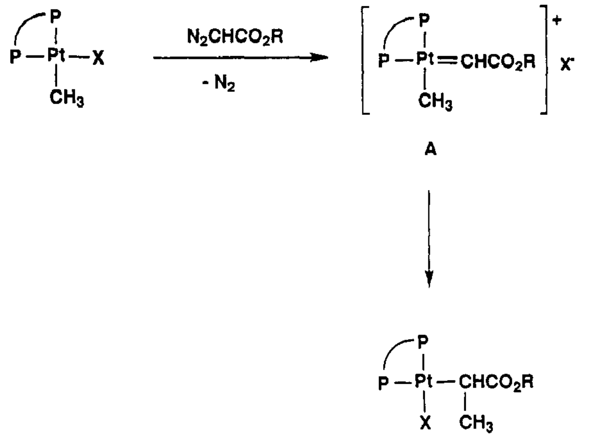
(7) The reaction of the achiral substrates [PtCl(CH_3)(dppp)] (dppp = 1,3-bis(diphenylphosphino)propane) and [PtCl(CH_3)(dppe)] (dppe = 1,2-bis(diphenylphosphino)ethane) with *R*-menthyl diazoacetate gave 1:1 mixtures of diastereomeric products, indicating that the chirality in the diazo ester does not have a significant effect on the diastereoselectivity. Nevertheless, as pointed out by one of the reviewers, it is still conceivable that *R*-menthyl diazoacetate is *matched* with **1a** but *mismatched* with **1a′** (using the nomenclature of Masamune et al.: *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1).

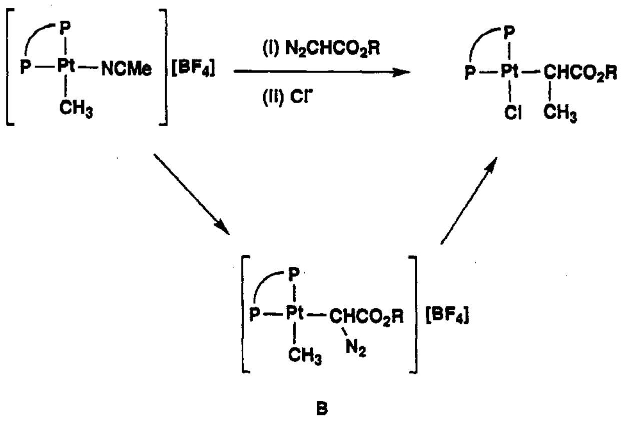
(8) The ratios of the diastereoisomers of Pt–X insertion are high: the iodo complexes **8c** and **9c** are detected in the ratio 12:1, while for the bromo complexes **8b** and **9b** only one isomer has been observed by NMR, implying a ratio of at least 20:1.

(9) Alkyl migration from metal to carbene is known to occur particularly readily when the complex is cationic; see for example: (a) Thorn, D. L.; Tulip, T. H. *J. Am. Chem. Soc.* **1981**, *103*, 5984. (b) McCrindle, R.; Arsenault, G. J.; Farwaha, R.; Hampden-Smith, M. J.; McAlees, A. J. *J. Chem. Soc., Chem. Commun.* **1986**, 943. (c) Hubbard, J. L.; Morneau, A.; Burns, R. M.; Nadeau, O. W. *J. Am. Chem. Soc.* **1991**, *113*, 9180.

Scheme 1



Scheme 2



(ii) the tendency for Pt–C insertion for the complexes [PtX(CH$_3$)(*S*,*S*-diop)] increases in the same order as the leaving-group ability of the halogen (I < Br < Cl); (iii) the ratio of the diastereoisomers formed is independent of the halogen. The possibility that the C–C bond-forming step involves the cationic diazoalkane complex **B** is not supported by the experiment shown in Scheme 2. Treatment of [Pt(CH$_3$)(NCMe)(*S*,*S*-diop)][BF$_4$] with N$_2$CHCO$_2$Et followed by addition of [AsPh$_4$]Cl gave, as expected, **2a** and **3a** presumably via the species **B**, but in the ratio 0.5:1,[10] which is quite different from the 2:1 ratio obtained in the direct reaction of [PtCl(CH$_3$)(*S*,*S*-diop)] with N$_2$CHCO$_2$Et (see above).

We have demonstrated that carbene insertions into Pt–C bonds can be diastereoselective. The details of the mechanism are still being elucidated, but on present evidence, the crucial C–C bond formation occurs by a methyl to carbene migration within a cationic complex.

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Supplementary Material Available: Text giving details of the synthesis and characterization of **2a**,**b**, **3a**,**b**, **8c**, and **9c**, tables giving elemental analysis and IR and ^{31}P NMR data for the complexes prepared in this paper, and details of the X-ray crystal structure study of **2a**, including tables of atomic coordinates, bond lengths and angles, and thermal parameters (10 pages). Ordering information is given on any current masthead page.

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[10] No significance is attached to this "inversion" of the product ratio from 2:1 to 1:2, because preliminary experiments have shown that no such inversion is observed in the reaction of *R*-menthyl diazoacetate with [Pt(CH$_3$)(NCMe)(*S*,*S*-diop)][BF$_4$] or [Pt(CH$_3$)(NCMe)(*R*,*R*-diop)][BF$_4$]: the products **4**, **5** and **6**, **7** were obtained (following addition of [AsPh$_4$]Cl) in the ratios 3:2 and 1:4, respectively (cf. 4:1 and 2:1 for the direct reaction of [PtCl(CH$_3$)(*S*,*S*-diop)] or [PtCl(CH$_3$)(*R*,*R*-diop)] with *R*-menthyl diazoacetate in MeCN).