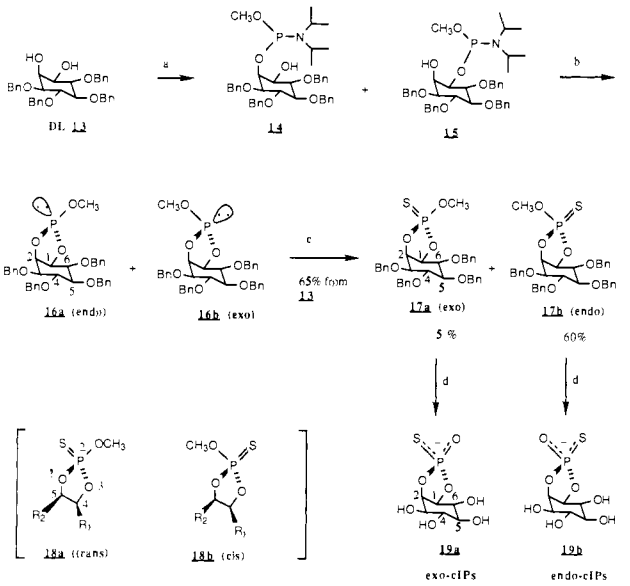
Scheme II. The Synthesis of Endo and Exo cIPs (DL Mixtures Were Used, but Only D-Forms Are Shown)[a]



[a] Reagents and conditions: (a) 1.2 equiv $ClP(OCH_3)N(iPr)_2$, iPr_2NEt, CH_2Cl_2, 25 °C, 0.5 h; (b) 4 equiv tetrazole, THF-CH_3CN, 25 °C, 18 h; (c) excess S_8, toluene, 25 °C, 48 h; (d) 40 equiv Li, THF-NH_3, -78 °C, 5 min.

cifically converts the R_p isomer of DPPsI to inositol 1,2-cyclic thiophosphate (cIPs) (**12**) (^{31}P δ 69.89 ppm, characteristic of cyclic thiophosphates) as the predominant product. Thus despite differences in substrate specificity, structure, and function, PI-PLC exhibits the same stereospecificity as phosphatidylcholine-specific PLC (PC-PLC), which prefers the S_p isomer of thiophosphatidylcholine.[10b-d]

To elucidate the steric course of PI-PLC requires cIPs with known configuration. Thus, DL-cIPs was synthesized according to Scheme II. DL-1,4,5,6-Tetra-*O*-benzyl-*myo*-inositol (**13**; prepared by established procedures[14]) was phosphorylated by $ClP(OCH_3)N(iPr)_2$ to give **14** and **15**, which were then treated with tetrazole in THF-CH_3CN to produce **16(a+b)** via a novel intramolecular cyclization.[15] Without isolation, **16** was treated with an excess of S_8 in toluene to give **17a** (^{31}P δ 84.41 ppm, *exo*-DL, i.e. D-R_p + L-S_p)[16] and **17b** (^{31}P δ 82.65 ppm, *endo*-DL, i.e. D-S_p + L-R_p), which were separated by chromatography. Assignments of the configurations of **17a** and **17b** were based on four criteria, the first three of which had been established previously on model compounds **18a**, **18b**, and related systems: (i) The predominant form **17b** should be endo since the predominant form of the phosphite **16** should be the least sterically hindered form **16b**,[17] and oxidation by sulfur is known to proceed with retention of configuration at phosphorus.[18] (ii) The relative ^{31}P δ of **17a** and **17b** thus assigned are consistent with that of **18a** and **18b** (83.0 and 80.5 ppm, respectively, when $R_1 = R_2 = CH_3$) in that the trans (exo) form is more downfield.[17b,19] (iii) The three-bond coupling constants between P and 1-H are 18.4 and 9.7 Hz for **17a** and **17b**, respectively. These are consistent with the data for **18a**, **18b**, and related compounds ($^3J_{H-C(4)-O-P}$ is **a** > **b**), and with the empirical rule that the OCH_3 group is "axial seeking" in these systems.[19,20] (iv) Irradiation of 2-H resulted in detectable nuclear Overhauser effect on the methyl proton resonance in **17b** but not **17a**. Detailed NMR assignments and conformational analysis will be presented later.

The synthesis was completed by treating **17a** and **17b** with Li in THF-NH_3(l) to give **19a** (exo[16], ^{31}P δ 69.85 ppm, Figure 1C) and **19b** (endo, ^{31}P δ 69.00 ppm, Figure 1D), respectively. The ^{31}P δ of **19a** coincides with that of **12**, which was further confirmed by addition of **19a** to the reaction mixture in Figure 1B (spectrum not shown). Thus the configuration of **12** should be D-R_p, and the steric course should be *inversion* at phosphorus. The result suggests that the conversion of PI to cIP catalyzed by PI-PLC from *B. cereus* involves direct attack of the 2-OH group to displace the diacylglycerol moiety of the substrate. The steric course of the formation of the noncyclic IP awaits future studies.

Application of phosphorothioates on PI-related systems has also been realized by other groups recently. Chemical synthesis of DL-cIPs[21] by a different procedure has been reported, but the configuration was not determined. The phosphorothioate analogues of DL-*myo*-inositol phosphates have been synthesized[22] and shown to be resistant to hydrolysis by phosphatases.[22c]

(13) The PI-PLC used in this work was obtained from Sigma (which consists of a mixture of PC-PLC, PI-PLC, and sphingomyelinase) and further purified by fast protein liquid chromatography. Sundler, R.; Alberts, A. W.; Vagelos, P. R. *J. Biol. Chem.* **1978**, *253*, 4175-4179.

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(15) To the best of our knowledge, this is the first example of using $ClP(OCH_3)N(iPr)_2$ as a phosphorylating and intramolecular cyclization agent.

(16) The exo form of **17** and **19** is defined as the form in which sulfur and the inositol ring are on the opposite side of the five-membered ring. In the *R/S* designation, the axial position has higher priority than the equatorial position when all things are equal.

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(22) (a) Cooke, A. M.; Gigg, R.; Potter, B. V. *J. Chem. Soc., Chem. Commun.* **1987**, 1525-1526. (b) Metschies, T.; Schultz, C.; Jastorff, B. *Tetrahedron Lett.* **1988**, *29*, 3921-3922. (c) Taylor, C. W.; Berridge, M. J.; Brown, K. D.; Cooke, A. M.; Potter, B. V. L. *Biochem. Biophys. Res. Commun.* **1988**, *150*, 626-632.

Novel Regioselectivity and C-F Bond Cleavage in the Reactions of Alkylplatinum(II) Complexes with Amide and Alkoxide Anions

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Received December 12, 1988

Recently there has been a surge of interest in the chemistry of complexes formed between amide or alkoxide anions and transition metals of the platinum group.[1] Previous synthesis had avoided such complexes because the "hard and soft" acid and base concept had predicted weak metal-ligand bonding. Recent solution equilibrium data, however, have shown that these complexes have bond enthalpies comparable with those of alkyl complexes.[2] This communication reports some novel regioselectivities discovered from reacting amides with platinum(II) complexes and

(1) Bryndza, H. E.; Tam, W. *Chem. Rev.* **1988**, *88*, 1163-1188.

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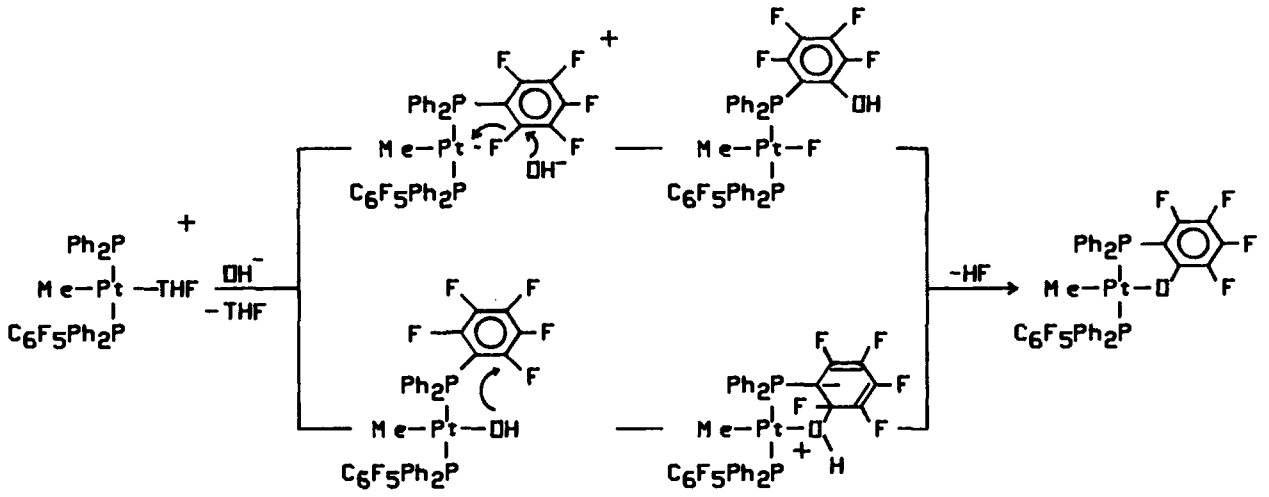
Scheme I



also describes products resulting from unanticipated C–F and C–O cleavage reactions.

The complex *trans*-$PtClMeL_2$ (L = PPh_3) reacts with OH^- or OMe^- to give *trans*-$Pt(OH)MeL_2$ and *trans*-$Pt(OMe)MeL_2$, respectively. The methoxide complex undergoes β-hydrogen transfer at elevated temperature to give *trans*-$PtHMeL_2$. By contrast *trans*-$Pt(OMe)(CF_3)L_2$ is stable because the electronegative CF_3 group enhances the π-stabilization of the Pt–OMe bond, thereby disfavoring β-hydrogen transfer.[3] Treating *trans*-$PtClMe(PCy_3)_2$ with $NaNH_2$ gives the amide complex *trans*-$Pt(NH_2)Me(PCy_3)_2$.[4] Thermodynamic considerations predict that the Pt–NMe_2 bond is weaker than either the Pt–NH_2 or the Pt–OMe bond,[2] and in agreement with this we observe *trans*-$PtHMeL_2$ as the reaction product from the reaction between *trans*-$PtClMeL_2$ (L = PPh_3, PCy_3) and $LiNMe_2$ in dry THF. Column chromatography of the product after a reaction time of 4 h gave 57% yield. For *trans*-$PtCl(CF_3)(PPh_3)_2$ we observe a different regioselectivity whereby

$$\textit{trans}\text{-}PtClMeL_2 + LiNMe_2 \rightarrow \textit{trans}\text{-}PtHMeL_2 + LiCl + MeN{=}CH_2 \quad (1)$$

(L = PPh_3, PCy_3)

attack of NMe_2^- at the trifluoromethyl ligand results in a complementary redox reaction to give $Pt(PPh_3)_3$ (eq 2).[5] We detect no $Pt(NMe_2)(CF_3)(PPh_3)_2$.

$$3\,\textit{trans}\text{-}PtCl(CF_3)(PPh_3)_2 + 3LiNMe_2 \rightarrow 2Pt(PPh_3)_3 + 3CF_3NMe_2 + 3LiCl + Pt \quad (2)$$

An alternate approach to π-stabilize metal alkoxides and amides is to use fluoro substituents on the tertiary phosphine rather than on the alkyl group. The complex *trans*-$PtClMe(PPh_2C_6F_5)_2$ is unreactive to OH^- or OMe^-, but *trans*-$[PtMe(THF)(PPh_2C_6F_5)_2]X$ (X = ClO_4, BF_4, CF_3SO_3) reacts with aqueous KOH (twofold excess) to give the cyclometalated complex *trans*-$PtMe(2\text{-}OC_6F_4PPh_2)(PPh_2C_6F_5)$ (**1**) (eq 3) in 68% yield after a reaction time of 30 min, followed by column chromatography.[6] The single-crystal structure of **1** gives the bond distances

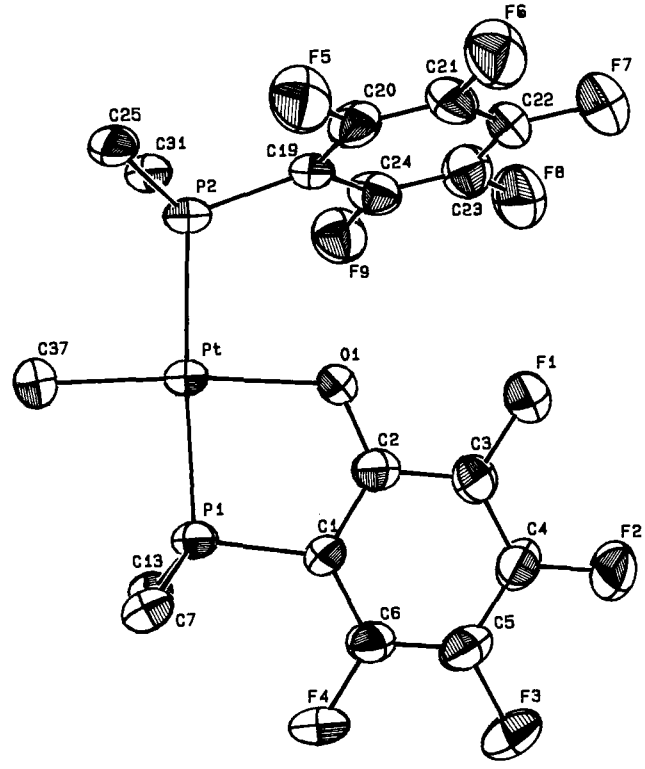
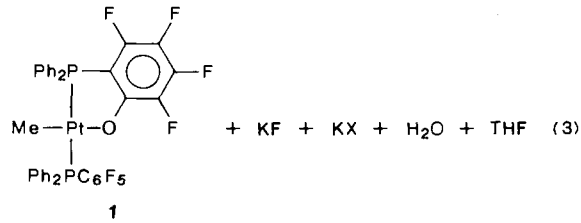


Figure 1. Molecular structure and atom labeling scheme for $C_{37}F_9OP_2PtH_{23}$ shown with 50% thermal ellipsoids. The C7–C18 and C25–C36 series phenyl rings bonded to P1 and P2 are shown as the ipso atoms only.

Pt–O1 = 2.12 (1) Å, Pt–C37 = 2.08 (1) Å, O1–C2 = 1.31 (1) Å. An ORTEP representation is shown in Figure 1.[7] This cy-



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(5) Chanon, M.; Tobe, M. L. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 1–23. We have independently prepared CF_3NMe_2 from CF_3I and $LiNMe_2$. The failure to observe CF_3H eliminates a pathway involving β-hydrogen transfer followed by reductive elimination from $PtH(CF_3)L_2$ (Michelin, R. A.; Belluco, U.; Ros, R. I. *Inorg. Chim. Acta* **1977**, *24*, L33–L34).

(6) ^1H, $^{31}P\{^1H\}$ and ^{19}F NMR data for **1**: δ (CH_3) 0.88 t; $^3J(PH)$ = 6.3 Hz. $\delta(P)$ 20.7 d, 31.9 d; $^2J(PP)$ = 448 Hz. δ (CF) –124 d (2 F), –132 d (1 F), –148 t (1 F), –151 t (1 F), –159 t (2 F), –163 d (1 F), –176 t (1 F); $^3J(FF)$ = 19–23 Hz.

(7) Crystal data: dimensions, 0.43 × 0.43 × 0.31 mm; crystal system, monoclinic; space group, $P2_1/c$; a = 12.437 (2) Å, b = 25.749 (8) Å, c = 10.788 (2) Å, β = 102.35 (1)°; Z = 4; absorption coefficient = 43.71 cm^{-1}; Mo Kα radiation with graphite monochromator; scan range 2θ = 1–50°; 5614 unique reflections with 3958 ≥ $3\sigma(I)$. Structure solution was obtained by direct methods and refined to convergence with full-matrix when R = 3.7, R_w = 5.5.

clometalated product results from nucleophilic atack by OH^- at the ortho carbon of a pentafluorophenyl ring. No reaction occurs between uncomplexed $PPh_2C_6F_5$ and aqueous KOH. The ortho substitution in complex **1** is therefore induced by platinum coordination. Two mechanistic pathways are plausible, each of which involves nucleophilic attack by hydroxide at the ortho carbon of the pentafluorophenyl ring (Scheme I). The first pathway involves an agostic interaction which induces ortho selectivity by the external nucleophile; the second pathway involves prior complexation of the hydroxide with platinum.[8] We presently have no conclusive evidence to differentiate between intramolecular or external attack at the ortho carbon by the hydroxyl nucleophile. Complex **1** is protonated by HCl to give the ring-opened complex *trans*-$PtClMe(PPh_2C_6F_5)(PPh_2C_6F_4OH\text{-}2)$ (**2**) (eq 4).

$$\textit{trans}\text{-}PtMe(2\text{-}OC_6F_4PPh_2)(PPh_2C_6F_5) + HCl \rightarrow \underset{\mathbf{2}}{\textit{trans}\text{-}PtClMe(PPh_2C_6F_5)(PPh_2C_6F_4OH\text{-}2)} \quad (4)$$

Methoxide ion (excess NaOMe in methanol) substitutes the fluorines at the ortho carbon atoms of the pentafluorophenyl ring in *trans*-$[PtMe(THF)(PPh_2C_6F_5)_2]CF_3SO_3$ to give *trans*-$Pt(OMe)Me(PPh_2C_6F_3(OMe\text{-}2,6)_2)_2$ (**3**) in 82% yield. Complex **3** reacts with NaOH to give *trans*-$PtMe(2\text{-}OC_6F_3(OMe\text{-}6)PPh_2)(PPh_2C_6F_3(OMe\text{-}2,6)_2)$ (**4**) (eq 5).[9] The conversion of **3**

$$\underset{\mathbf{3}}{\textit{trans}\text{-}[PtMe(THF)(PPh_2C_6F_5)_2]X} + 5NaOMe \longrightarrow \textit{trans}\text{-}Pt(OMe)Me(PPh_2C_6F_3(OMe\text{-}2,6)_2)_2 + NaX +$$

$$4NaF \xrightarrow[OH^-]{-OMe^-} \underset{\mathbf{4}}{Me\text{-}Pt(PPh_2C_6F_3(OMe\text{-}2,6)_2)\text{-}O\text{-}C_6F_3(OMe\text{-}2,6)PPh_2} \quad (5)$$

$(X = CF_3SO_3)$

to **4** involves C–O bond cleavage.[10] These reactions involve the conversion of a strong C–F bond into a weaker C–O bond. The formation of platinum alkoxide bonds in both **3** and **4** provides some driving force to the reaction, but solvation effects and the higher lattice energy of NaF as compared to NaOMe provide the dominant advantage.

Acknowledgment. We thank the Louisiana Board of Reagents for support and Mark Fink for helpful discussions.

Supplementary Material Available: Tables of positional parameters, bond distances, bond angles, general displacement parameters, and torsion angles (13 pages); listing of observed and calculated structure factors (40 pages). Ordering information is given on any current masthead page.

(8) Although we have no direct evidence for an agostic interaction, precedents exist for both organohalide complexation and C–F cleavage and oxidative addition, see: Richmond, T. G.; Osterberg, C. E.; Arif, A. M. *J. Am. Chem. Soc.* **1987**, *109*, 8091–8092. Crabtree, R. H.; Faller, J. W.; Mellea, M. F.; Quirk, J. M. *Organometallics* **1982**, *1*, 1361–1366. Crabtree, R. H.; Mellea, M. F.; Quirk, J. M. *J. Am. Chem. Soc.* **1984**, *106*, 2913–2917. Gross, M. E.; Johnson, C. E.; Maroney, M. J.; Trogler, W. C. *Inorg. Chem.* **1984**, *23*, 2968–2973. For nucleophilic substitution of fluoroaromatics see: Tatlow, J. C. *Endeavour* **1963**, *22*, 89–95. Allen, J. G.; Burdon, J.; Tatlow, J. C. *J. Chem. Soc.* **1965**, 1045–1051. Banks, R. E. *Fluorocarbons and their Derivatives*, 2nd ed.; MacDonald: London, 1970; pp 218–221. Attack by external nucleophile is favored by the observation that no reaction occurs with NaOH instead of KOH, but prior hydroxyl coordination better explains the *ortho* selectivity. An $S_{RN}1$ mechanism fails to explain the selectivity, and futhermore **1** is not formed in the reaction between *trans*-$[PtMe(THF)(PPh_2C_6F_5)_2]X$ and sodium naphthalenide.

(9) ^1H, $^{31}P\{^1H\}$, and ^{19}F NMR data for **3**: δ (CH_3) 0.23 t; $^3J(PH)$ = 6.4 Hz. $\delta(OCH_3)$, 3.32 d (12 H); $^5J(HF)$ = 2.4 Hz. $\delta(OCH_3)$ 3.14 s (3 H); $^3J(PtH)$ = 23 Hz. $\delta(P)$ 16.7 s; $^1J(PtP)$ = 3527 Hz. $\delta(CF)$ -151.6 t (2 F), -155.8 d (4 F); $^3J(FF)$ = 20.3 Hz. **4**: δ (CH_3) 0.83 dd; $^3J(PH)$ = 7.0 Hz, $^3J(PH)$ = 5.5 Hz. δ (OCH_3) 3.23 d (6 H); $^5J(HF)$ = 2.5 Hz. δ (OCH_3) 3.00 d (3 H); $^5J(HF)$ = 2.7 Hz. δ (*P*) 33.8 d, 20.7 d; $^2J(PP)$ = 442 Hz. δ (*CF*) -150.7 t (1 F), -152.1 t (1 F), -155.6 d (2 F), -163.7 d (1 F), -169.6 d (1 F); $^3J(FF)$ = 20.5 Hz.

(10) A similar C–O cleavage reaction has been published, see: Jones, C. E.; Shaw, B. L.; Turtle, B. L. *J. Chem. Soc., Dalton Trans.* **1974**, 992–999.

First Structural Evidence for Transannular P–N Bonding in the Phosphine Form of Cyclenphosphorane: An Open Tautomer?

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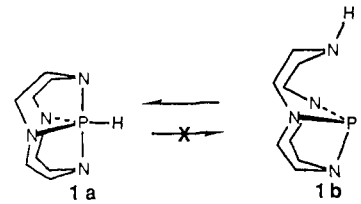
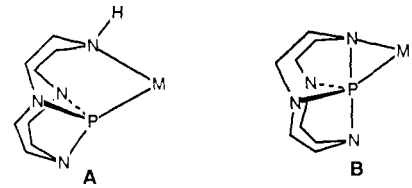
Received December 12, 1988

Evidence has shown that cyclenphosphorane (cyclenPH) exists only in the "closed" tautomer **1a** in solution as well as in the solid



(1)

and gas phases.[1] Attempts to isolate the "open" form **1b** by coordination to transition metals have, thus far, been unsuccessful, except in the rare cases where it is forced into the bidentate structure A.[2] Reactions of cyclenPH with transition metals usually give the pentacoordinate structure B.[3] It has been sug-



gested that this is due to the constraint of the 12-membered cyclen ring which stabilizes the trigonal-bipyramidal (tbp) geometry around phosphorus.[3,4] We herein report the synthesis and X-ray crystal structure of the first monodentate P-bound transition-metal complex of **1b**. The structure of this complex reveals a P–N transannular interaction, which yields a unique geometry for a phosphine ligand, and provides the first structural confirmation of the tbp constraining "bite" of the cyclen ring about phosphorus. Moreover, the geometry explains why this complex undergoes a

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(1) (a) Atkins, T. J.; Richman, J. E. *Tetrahedron Lett.* **1978**, 5149. (b) Richman, J. E.; Atkins, T. J. *Tetrahedron Lett.* **1978**, 4333.

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