Access to Phosphacymantrene-2-carboxylic Acid and 2-Carboxaldehyde Derivatives

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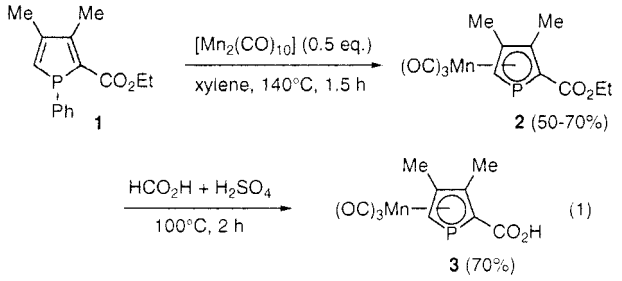
Two new approaches to α-functional phosphacymantrenes are described. The reaction of $[Mn_2(CO)_{10}]$ with a phosphole-2-carboxylate affords the corresponding phosphacymantrene-2-carboxylate **2**. Replacing one carbonyl by one triphenylphosphine on manganese enhances the reactivity of phosphacymantrenes toward electrophilic substitution. Thus, a Vilsmeier formylation leading to a phosphacymantrene-2-carboxaldehyde such as **5** becomes possible. The reduction of **5** affords the corresponding primary alcohol **6** and the methyl derivative **7**.

Introduction

Enantiopure planar-chiral ferrocenylphosphines play a central role in asymmetric catalysis.[1] As a logical extension of the same concepts, several promising studies have been recently published on planar-chiral phosphaferrocenes.[2,3] From a synthetic standpoint, the access to these molecules critically depends on the straightforward preparation of phosphaferrocene-2-carboxaldehydes by a simple Vilsmeier formylation.[4] Even more recently, our attention was caught by a report of Kudis and Helmchen describing the first successful applications of enantiopure planar-chiral cymantrenylphosphines in asymmetric catalysis.[5] Put together, all these data led us to envisage the possible use of the readily available phosphacymantrenes[6] in the same area. Unfortunately, only Friedel−Crafts acylations are possible with these species,[7] and both the 2-carboxylic acid and 2-carboxaldehyde derivatives are presently unknown. Thus, it appeared necessary to break this synthetic bottleneck.

Results and Discussion

We first decided to investigate the reaction of $[Mn_2(CO)_{10}]$ with some 2-functional 1-phenylphospholes. Our first choice was the readily available 1-phenyl-2-ethoxycarbonyl-3,4-dimethylphosphole **1**.[8] A careful optimization of the reaction conditions allowed us to obtain the corresponding phosphacymantrene **2** in 50−70% yield (eq 1).



Two observations need further comments. First, it is necessary to use 0.5 equiv of $[Mn_2(CO)_{10}]$ to obtain the best results. Any excess results in lower yields. This observation is consistent with a radical mechanism involving a mononuclear species such as $[Mn(CO)_4]^\bullet$. The intervention of such a species at 140 °C is conceivable since both D(Mn−Mn) and D(Mn−CO) are low and approximately equal at 36−38 kcal mol^{-1}.[9] After coordination of $[Mn(CO)_4]^\bullet$ at P, a further loss of CO and the expulsion of a phenyl radical would complete the process. Of course, this mechanism is purely speculative at the moment. Second, the functional phosphacymantrene **2** is extremely sensitive toward nucleophiles. It is necessary to use a preacidified silica gel column to obtain satisfactory results during the purification process. Conversely, the resistance of **2** toward acidic media is quite good. The acid hydrolysis of **2** at 100 °C indeed affords the corresponding carboxylic acid **3** in good yield.

The sensitivity of **2** toward nucleophiles combined with the relative inertness of the carboxylate functionality led us to investigate the synthesis of other functional phosphacymantrenes. A transposition of the synthesis of **2** with the 2-formylphosphole proved unsuccessful. We reasoned that the failure of the Vilsmeier formylation with phosphacymantrenes was due to the

(1) The main application of such phosphines is certainly the production of the herbicide (*S*)-metolachlor in quantities of 10 000 tons per year; see: Togni, A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1475.
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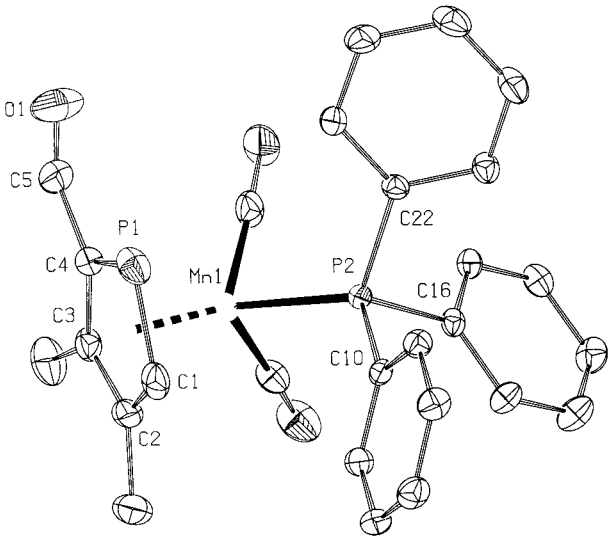
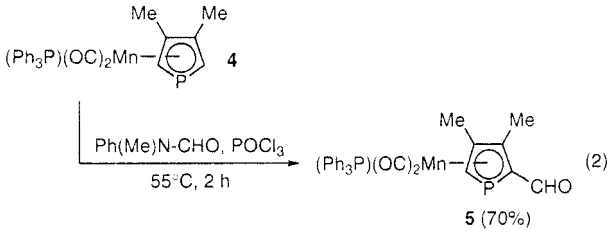


Figure 1. X-ray crystal structure of **5**. Selected bond lengths (Å) and angles (deg.): P(1)−C(1) 1.767(5), P(1)−C(4) 1.792(5), C(1)−C(2) 1.382(7), C(2)−C(3) 1.443(6), C(3)−C(4) 1.420(6), C(4)−C(5) 1.456(7), O(1)−C(5) 1.190(7), Mn(1)−P(1) 2.420(1), Mn(1)−P(2) 2.254(1), Mn(1)−CO 1.777(5) and 1.784(4); C(1)−P(1)−C(4) 86.8(2), OC−Mn(1)−CO 91.2(2), P(2)−Mn(1)−CO 90.1(1) and 90.3(1), P(2)−Mn(1)−P(1) 97.61(5).

high electron-withdrawing power of the $[Mn(CO)_3]$ complexing group. We supposed that the substitution of one CO by a phosphine ligand would increase the sensitivity of the phospholyl toward electrophilic attack. Indeed, a Vilsmeier formylation was successfully performed with the substituted phosphacymantrene **4**[10] (eq 2).



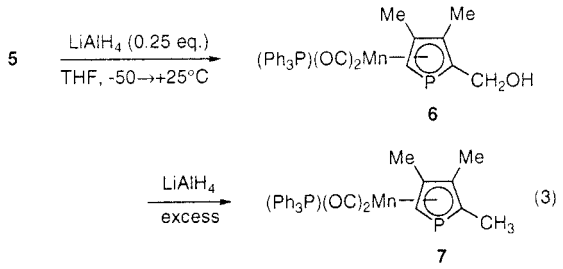
The crystal structure of **5** is shown in Figure 1. The aldehyde group is almost coplanar with the phospholyl ring (P(1)−C(4)-C(5)−O(1) dihedral angle = 2.1°) and the carbonyl is syn to the ring phosphorus. The Ph_3P−Mn(1)−centroid plane bisects the P(1)−C(1) unsubstituted ring bond in order to minimize steric repulsion. Otherwise, the structure is very similar to that already published for a 2-benzoylphosphacymantrene.[7]

As expected, the aldehyde is an efficient starting point for the synthesis of other functional derivatives. Its reduction by a stoichiometric amount of $LiAlH_4$ at low temperature affords the alcohol **6**, whereas an excess leads to the methyl derivative **7** (eq 3).

The mechanism of formation of **7** is presently unclear. With functional derivatives such as **2** and **5**, we are now able to develop the chemistry of phosphacymantrenes.

Experimental Section

All reactions were performed under nitrogen; the solvents were purified, dried, and degassed by standard techniques. ^1H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker AC 200 SY spectrometer operating at 200.13, 50.32, and 81.01 MHz, respectively. All chemical shifts are reported in ppm downfield from internal TMS (^1H and ^{13}C) and external 85% H_3PO_4 (^{31}P). Mass spectra (EI) were obtained at 70 eV by the direct inlet method.



2-Ethoxycarbonyl-3,4-dimethylphosphacymantrene 2. Phosphole **1** (1 g, 3.8×10^{-3} mol) and $[Mn_2(CO)_{10}]$ (0.75 g, 1.9×10^{-3} mol) were heated at 140 °C for 1.5 h in 15 mL of xylene. After cooling and evaporation of the solvent, the residue was chromatographed on silica gel (Merck 60, 0.063−0.200 mm). Before use, the silica gel was treated by a HCl solution in ether in order to destroy the basic sites. Elution with hexane, then with 70:30 hexane/dichloromethane, afforded **2** as a yellow oil in 50−70% yields (0.6−0.85 g). ^{31}P NMR ($CDCl_3$): δ −23. ^1H NMR ($CDCl_3$): δ 1.28 (t, 3H, CH_3(Et)), 2.17 (s, 3H, Me), 2.46 (s, 3H, Me), 4.16 (m, 2H, CH_2(Et)), 4.69 (d, 1H, $^2J_{H-P}$ = 32.1 Hz, CH−P). ^{13}C NMR ($CDCl_3$): δ 13.56 (s, CH_3(Et)), 14.03 (s, CH_3), 15.48 (s, CH_3), 60.97 (s, CH_2(Et)), 95.59 (d, $^1J_{C-P}$ = 61.2 Hz, =*C*−COOEt), 99.40 (d, $^1J_{C-P}$ = 62.0 Hz, P−C−H), 118.80 (d, $^2J_{C-P}$ = 7.9 Hz, *C*−CH_3), 115.70 (d, $^2J_{C-P}$ = 5.8 Hz, *C*−CH_3), 167.10 (d, $^2J_{C-P}$ = 18.5 Hz, COOEt), 222.54 (s, CO). Mass: *m*/*z* 323 (M^+ + 1, 14), 322 (M^+, 13), 266 (M^+ − 2CO, 10), 238 (M^+ − 3CO, 51.6), 194 (M^+ + H − 3CO − OEt, 100). Anal. Calcd for $C_{12}H_{12}MnO_5P$: C, 44.72; H, 3.73. Found: C, 46.09; H, 3.73.

3,4-Dimethylphosphacymantrene-2-carboxylic Acid 3. Ester **2** (1 g, 3.1×10^{-3} mol) was heated at 100 °C for 2 h in a mixture of formic acid (8 mL) and sulfuric acid (2 mL). After cooling, the crude mixture was extracted with chloroform. After evaporation, the acid **3** was precipitated in toluene; 0.45−0.65 g was isolated (yield 50−70%). ^{31}P NMR (CD_3OD): δ −22.2. ^1H NMR (CD_3OD): δ 2.17 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 4.88 (d, 1H, $^2J_{H-P}$ = 35.3 Hz, P−C−H). ^{13}C NMR (CD_3OD): δ 13.77 (s, CH_3), 15.55 (s, CH_3), 97.20 (d, $^1J_{C-P}$ = 61.0 Hz, *C*−COOH), 100.57 (d, $^1J_{C-P}$ = 61.5 Hz, P−C−H), 114.32 (d, $^2J_{C-P}$ = 13.1 Hz, *C*−CH_3), 117.27 (d, $^2J_{C-P}$ = 5.9 Hz, *C*−CH_3), 170.18 (d, $^2J_{C-P}$ = 22.8 Hz, COOH), 221.11 (s, CO). IR (decalin): ν max 2027.8, 1960.6, 1950.3 cm^{-1} (CO). Mass: *m*/*z* 294 (M^+, 11.7), 238 (M^+ − 2CO, 11.7), 237 (M^+ −2CO −H), 8.5), 210 (M^+ −3CO, 100). Anal. Calcd for $C_{10}H_8MnO_5P$: C, 40.81; H, 2.72. Found: C, 39.98; H, 2.72.

[(η^5-2-Formyl-3,4-dimethylphospholyl)(triphenylphosphine)]manganesedicarbonyl 5. A mixture of **4**[10] (1.0 g, 2×10^{-3} mol), freshly distilled $POCl_3$ (0.4 mL), and *N*-methyl-*N*-phenylformamide (0.5 g) in dichloromethane (10 mL) was heated at 55 °C for 2 h. After hydrolysis and neutralization with CO_3Na_2, the CH_2Cl_2 layer was dried over magnesium sulfate and evaporated. The residue was chromatographed on silica gel with hexane/CH_2Cl_2 (70:30) as the eluent; 0.75 g of **5** was isolated as a orange powder (yield 70%). ^{31}P NMR ($CDCl_3$): δ 86.0 (s, PPh_3), −19.8 (s, cyclic P). ^1H NMR (CD_2Cl_2) δ 1.94 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 4.55 (dd, 1H, $^2J_{H-P}$ =35.8 Hz, $^4J_{H-P}$ = 2.4 Hz, =C−H), 8.84 (d, $^3J_{H-P}$ = 4.2 Hz, CHO). ^{13}C NMR (CD_2Cl_2) δ 13.80 (s, CH_3), 15.36 (s, CH_3), 101.52 (d, $^1J_{C-P}$ = 59.9 Hz, C−P cycle), 108.82 (d, $^2J_{C-P}$ = 4.6 Hz, *C*-CH_3), 112.83 (d, $^2J_{C-P}$ =7.6 Hz, *C*−CH_3), 192.82 (d, $^2J_{C-P}$ = 26.70 Hz, CHO), 230.40 (m, CO). Mass: *m*/*z* 512 (M^+, 2.5), 456 (M^+ − 2CO, 100), 194 (M^+ − Ph_3P − 2CO, 24.4). Anal. Calcd for $C_{27}H_{23}MnO_3P_2$: C, 63.29; H, 4.52. Found: C, 62.50; H, 4.92.

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[(η^5-2-Hydroxymethyl-3,4-dimethylphospholyl)(triphenylphosphine)]manganesedicarbonyl 6. To a solution of **5** (1.0 g, 1.95×10^{-3} mol) in THF (10 mL) cooled at −50 °C was added with a syringe 0.3 mL (0.5×10^{-3} mol) of a 1 M solution of $LiAlH_4$ in THF. The reaction mixture was allowed to warm to room temperature and hydrolyzed. After extraction with CH_2Cl_2 and chromatography on silica gel with 90:10 CH_2Cl_2/AcOEt, 0.6−0.8 g of **6** was isolated as a yellow powder (yield 80%). ^{31}P NMR (CH_2Cl_2): δ 89.9 (s, PPh_3), −43.3 (s, cyclic P). ^{1}H NMR δ 1.90 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 3.49 (dd, 1H, $^2J_{H-P}$ = 35.1 Hz, $^4J_{H-P}$ = 4.4 Hz, P−C−H), 4.25 (m, 2H, CH_2OH). ^{13}C NMR δ 12.22 (s, CH_3), 15.12 (s, CH_3), 60.67 (d, $^2J_{C-P}$ = 20.9 Hz, CH_2OH), 97.51 (d, $^2J_{C-P}$ = 59.7 Hz, H−C−P cycle), 103.72 (d, $^2J_{C-P}$ = 4.9 Hz, *C*−CH_3), 111.16 (d, $^2J_{C-P}$ =7.0 Hz, *C*−CH_3), 113.82 (d, $^1J_{C-P}$ =56.6 Hz, *C*−CH_2OH), 231.0 (m, CO). Mass: *m*/*z* 514 (M^+, 1.0%), 456 (M^+ − 2CO, 29.3). Anal. Calcd for $C_{27}H_{25}MnO_3P_2$: C, 63.05; H, 4.90. Found: C, 62.68; H, 4.76.

[(η^5-2,3,4-Trimethylphospholyl)(triphenylphosphine)]manganesedicarbonyl 7. The same reaction was run with 4-fold excess of $LiAlH_4$. The product was eluted with hexane/CH_2Cl_2 (90:10) (yield 70%). ^{31}P NMR (CH_2Cl_2): δ +89.0 (PPh_3), −45.0 (cyclic P). ^{1}H NMR (CH_2Cl_2) δ 1.80 (d, 3H, $^3J_{H-P}$ = 9.5 Hz, P−C−CH_3), 1.91 (s, 3H, CH_3), 2.00 (s, 3H, CH_3), 3.23 (dd, 1H, $^2J_{H-P}$ = 34.1 Hz, $^4J_{H-P}$ = 4.1 Hz, P−C−H), 7.36−7.52 (m, Ph). ^{13}C NMR ($CDCl_3$): δ 11.91 (s, CH_3), 14.61 (d, $^2J_{C-P}$ =25.9 Hz, CH_3), 15.20 (s, CH_3), 95.39 (d, $^1J_{C-P}$ = 59.4 Hz, H−C−P cycle), 102.93 (d, $^2J_{C-P}$ = 4.0 Hz, *C*−CH_3), 109.96 (d, $^2J_{C-P}$ =6.1 Hz, *C*−CH_3), 112.08 (d, $^1J_{C-P}$ = 55.3 Hz, P−*C*−CH_3), 231.0 (m, CO). Mass: *m*/*z* 498 (M^+, 3), 442 (M^+ − 2CO, 100).

Crystallographic Data for 5. $C_{27}H_{23}MnO_3P_2$: M = 512.33 g/mol; monoclinic; space group $P2_1/n$; a = 10.1400(6) Å, b = 16.0040(8) Å, c = 14.6200(7) Å, β = 97.532(3)°, V = 2352.1(2) Å^3; Z = 4; D = 1.447 g cm^{-3}; m = 0.725 cm^{-1}; F(000) = 1056. Crystal dimensions 0.18 × 0.14 × 0.10. Total reflections collected 17480 and 4215 with $I > 2\sigma(I)$. Goodness of fit on F^2 1.094; $R(I > 2\sigma(I))$ = 0.0665, wR2 = 0.1678 (all data); maximum/minimum residual density 2.219(0.095)/−0.947(0.095) e Å^{-3}. Data were collected on a KappaCCD diffractometer at 150(1) K with Mo Kα radiation (λ = 0.71073 Å). Full details of the crystallographic analysis are described in the Supporting Information.

Supporting Information Available: For **5**, tables of additional crystal data collection and refinement parameters, atomic coordinates, thermal parameters, and complete tables of distances and angles are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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