Notes

Electrophilic Alkylation of Electron-Rich Arenes by Phosphacymantrenylcarbenium Ions

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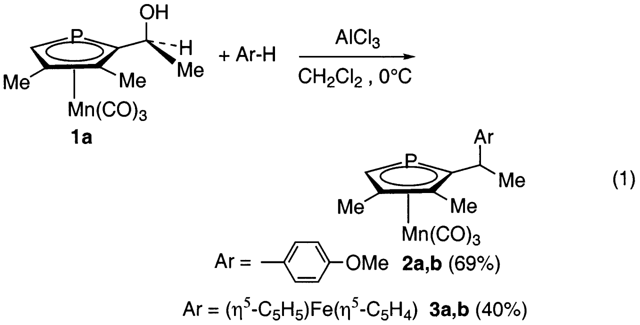
*Summary: Phosphacymantren-2-ylcarbinol **1** is transformed into the corresponding carbenium ion by reaction with $AlCl_3$ in CH_2Cl_2 at 0 °C. This ion is able to alkylate ferrocene and electron-rich arenes such as anisole and 1,3-dimethoxybenzene. One isomer of the double-alkylation product derived from 1,3-dimethoxybenzene has been characterized by X-ray crystal structure analysis. It derives from the carbenium ion with the E-stereochemistry.*

Introduction

Recent work by Ganter[1] has demonstrated that the replacement of an η^5-cyclopentadienyl ligand by an η^5-phospholyl group does not significantly alter the ability of a ferrocene derivative to stabilize a ferrocenylcarbenium ion. It is also known from pK_{R+} measurements[2] that benchrotrenyl- and cymantrenylcarbenium ions display almost equal stabilities. Despite their stabilization by the $[Cr(CO)_3]$ group, benchrotrenylcarbenium ions remain sufficiently electrophilic to alkylate electron-rich arenes, and this property has found some use in organic synthesis.[3] These various data led us to wonder whether the phosphacymantrenylcarbenium ions could enter into a similar chemistry with electron-rich arenes, thus providing an access to hitherto unaccessible phosphole-containing molecules.

Results and Discussion

All our experiments were conducted with the easily available secondary phosphacymantrenylcarbinol **1**.[4] Compound **1** is prepared by reduction of the corresponding 2-acetyl derivative by $NaBH_4$ in ethanol and is obtained as a 85:15 mixture of two diastereomers: $\delta\,^{31}P$ −48.2 (major) and −41.4 (minor) in $CDCl_3$. The more shielded major isomer **1a** is assigned the configuration shown in eq 1 by analogy with the work of Ganter on the analogous phosphaferrocene derivative.[1] The test reaction was conducted with anisole. Using $AlCl_3$ as the Lewis acid, the expected *para*-alkylation product **2** was obtained in satisfactory yield (eq 1).



1a

(1)

2a,b (69%)

Ar = $(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4)$ **3a,b** (40%)

Other Lewis acids such as H_2SO_4 or HBF_4 are also effective, but $F_3B{\cdot}OEt_2$, $ZnCl_2$, and CF_3SO_3H proved to be useless. Compound **2** was obtained as a 80:20 mixture of two diastereomers ($\delta\,^{31}P$ −40.1 (**2a**, major), −31.7 (**2b**, minor) ($CDCl_3$)), which could not be separated. Mass spectrometry confirmed the formulation of **2** (*m*/*z* 384, M^+), and a complete characterization of each isomer by ^1H and ^{13}C NMR spectroscopy proved possible. The most striking difference between the spectra of both compounds concerns the ^1H resonance of the methyl group located on the β-carbon of the phospholyl ring. In **2a** (major), it is found at higher field, δ Me(β) 1.75, δ Me(β') 2.01; in **2b** (minor), δ Me(β) 2.07, δ Me(β') 2.14. The stereochemical origin of this effect will be discussed later.

We then attempted to reproduce this reaction using ferrocene in place of anisole. Once again, two isomers were obtained ($\delta\,^{31}P$ −35.1 (**3a**, 80%), −28.8 (**3b**, 20%)), and the major isomer shows some shielding of the methyl protons on C_β (**3a**, δ Me(β) 1.99, δ Me(β') 2.07; **3b**, δ Me(β) 2.05, δ Me(β') 2.10).

The next step was an application of this methodology to build a more sophisticated, potentially chelating, bisphosphacymantrenyl structure. The attempt was carried out with 1,3-dimethoxybenzene (eq 2).

Here of course, with two chiral sp^3-carbons and two planar chiral η^5-units, several diastereomers should be formed, and these were indeed observed when monitoring the reaction mixture by ^{31}P NMR. We were able to isolate the two major ones, **4a** and **4b**, in the pure state by chromatography on silica gel. Both feature the high

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[1] Brassat, L.; Ganter, B.; Ganter, C. *Chem. Eur. J.* **1998**, *4*, 2148.

[2] Watts, W. E. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 8, p 1052.

[3] Davies, S. G.; Donohoe, T. J. *Synlett* **1993**, 323.

[4] Breque, A.; Mathey, F.; Santini, C. *J. Organomet. Chem.* **1979**, *165*, 129.

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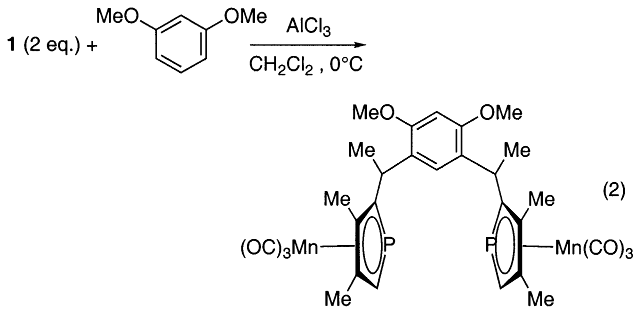


4a,b + minor isomers
overall yield 70 %

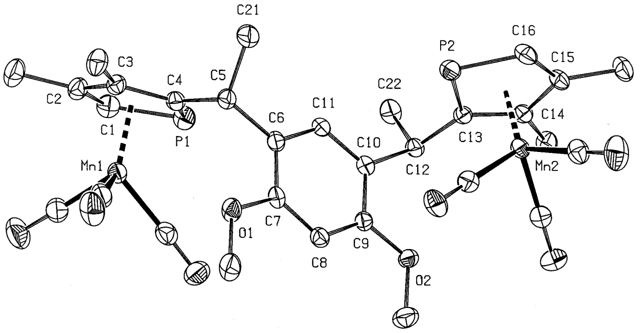
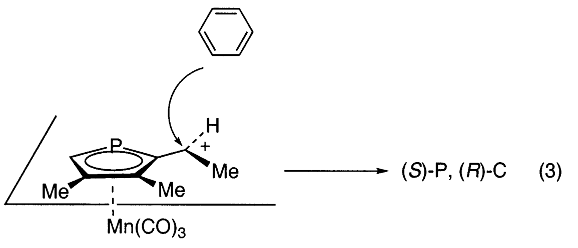


Figure 1. Crystal structure of **4b**.

field shifted Me(β) protons already observed for **2a** and **3a**. We have been able to get good crystals of **4b** and to determine its X-ray crystal structure (Figure 1). Given the high degree of steric crowding and restricted rotation, this structure is probably not very different from the structure in solution. On this basis, the shielding of the Me(β) protons could result from a through-space interaction with the methyl groups of the CHMe linkers. From another standpoint, the two former phosphacymantrenylcarbenium units in **4b** (P_1, C_5) and (P_2, C_{12}) display the (*S*)-P, (*R*)-C or (*R*)-P, (*S*)-C stereochemistry. If we admit, for obvious steric reasons, that the electron-rich arene attacks the carbenium ion from the *exo*-side, the carbocation (*Z*)-**5** will give the diastereomeric unit with the (*R*)-P, (*R*)-C + (*S*)-P, (*S*)-C stereochemistry, whereas (*E*)-**5** will give the observed stereochemistry (eq 3).



(*E*)-**5**

Cation (*E*)-**5** is probably formed by abstraction of OH$^-$ from **1a** on the *exo*-side (see the work of Ganter on the analogous phosphaferrocenylcarbenium ions).[1] Quite logically, (*E*)-**5** is less stable than (*Z*)-**5**, and thus our observation means that the rate of the reaction of (*E*)-**5** with the electron-rich arene is higher than the rate of the conversion of (*E*)-**5** into (*Z*)-**5**. From a purely practical standpoint, the synthesis of **4a**,**b** opens the possibility of synthesizing various flexible rings containing several phosphole units.[5] Only a few such species are presently known.[6]

Experimental Section

NMR spectra were recorded on a multinuclear Bruker AVANCE 300 MHz spectrometer operating at 300.13 for ^{1}H, 75.47 for ^{13}C, and 121.50 MHz for ^{31}P. Chemical shifts are expressed in parts per million (ppm) downfield from internal tetramethylsilane (^{1}H and ^{13}C) and external 85% aqueous H_3PO_4(^{31}P). Elemental analyses were performed by the Service de microanalyse du CNRS, Gif-sur-Yvette, France. High-resolution mass spectra were recorded by Service de spectrométrie de masse, Département de chimie, Ecole Normale Supérieure, Paris, France.

2-(4′-Methoxyphenyl)ethyl-3,4-dimethylphosphacymantrene, 2. 2-(1′-Hydroxyethyl)-3,4-dimethylphosphacymantrene, **1** (300 mg, 1 mmol), and 108 mg of anisole (1 mmol) were placed in a Schlenk tube under nitrogen atmosphere, and 20 mL of distilled dichoromethane was added via a septum. The yellow solution was cooled to 0 °C, and 145 mg of aluminum chloride (1 mmol) was added. The solution turned dark brown after 15 min. The consumption of the starting phosphacymantrene was monitored by ^{31}P NMR spectroscopy after 2 h of reaction. The reaction medium was diluted by 50 mL of dichloromethane, and the solution was hydrolyzed using 100 mL of a saturated sodium hydrogen carbonate aqueous solution and washed with 100 mL of brine. The organic layer was collected and dried with magnesium sulfate, and the solvents were removed under vacuum to give the crude products as an orange oil. Chromatography over silica gel was carried out with a 90:10 hexane/ether mixture as the eluent. The two diastereoisomers **2a** and **2b** (265 mg) of the final product were isolated as a mixture (80:20): 69% yield; MS *m*/*z* 384 (M^+, 10), 300 ($M^+ - 3CO$, 100), 245 ($M^+ - 3CO - Mn$, 11); HRMS for the mixture **2a**+**2b** calcd 384.0323, found 384.0320.

2a: ^{1}H NMR ($CDCl_3$) δ 1.34 (d, $^4J_{H-P} = 7$ Hz, 3H, benzylic CH_3), 1.75 (s, 3H, C_β-CH_3), 2.01 (s, 3H, C_β-CH_3), 3.41 (m, 1H, benzylic proton), 3.69 (s, 3H, CH_3-O), 4.12 (d, $^2J_{H-P} = 36$ Hz, 1H, C^5-H), 6.73 (d, $^3J_{H-H} = 8$ Hz, 2H, $C^{2'}$-H), 7.03 (d, $^3J_{H-H} =$ 8 Hz, 2H, $C^{3'}$-H); {^{1}H}^{13}C NMR ($CDCl_3$) δ 13.61 (s), 16.41 (s), 25.26 (d, $^3J_{C-P} = 17$ Hz, benzylic CH_3), 40.50 (d, $^2J_{C-P} = 13$ Hz, benzylic C), 55.85 (s, CH_3-O), 90.78 (d, $^1J_{C-P} = 59$ Hz, C^5), 109.85 (d, $^2J_{C-P} = 6$ Hz, C^4), 114.54 (s, C_{meta}), 115.17 (d, $^2J_{C-P}$ $= 6$ Hz, C^3), 128.70 (s, C_{ortho}), 138.27 (s, C_{ipso}), 158.66 (s, C_{para}), 225.05 (s, CO); {^{1}H}^{31}P NMR ($CDCl_3$) δ −40.14.

2b: ^{1}H NMR ($CDCl_3$) δ 1.39 (d, $^4J_{H-P} = 7$ Hz, 3H, benzylic CH_3), 2.07 (s, 3H, C_β-CH_3), 2.14 (s, 3H, C_β-CH_3), 3.41 (m, 1H, benzylic proton), 3.72 (s, 3H, CH_3-O), 4.17 (d, $^2J_{H-P} = 36$ Hz, 1H), 6.79 (d, $^3J_{A-B} = 8$ Hz, 2H, $C^{2'}$-H), 7.14 (d, $^3J_{A-B} = 8$ Hz, 2H, $C^{3'}$-H); {^{1}H}^{13}C NMR ($CDCl_3$) δ 13.55 (s), 16.45 (s), 24.79 (s, benzylic CH_3), 39.97 (d, $^2J_{C-P} = 15$ Hz, benzylic C), 55.85 (s, CH_3-O), 91.11 (d, $^1J_{C-P} = 60$ Hz, C^5), 110.71 (d, $^2J_{C-P} = 6$ Hz, C^4), 113.75 (d, $^2J_{C-P} = 6$ Hz, C^3), 114.16 (s, C_{meta}), 129.66 (d, $J = 4$ Hz, C_{ortho}), 136.90 (d, $J = 3$ Hz, C_{ipso}), 159.20 (s, C_{para}), 225.05 (s, CO); {^{1}H}^{31}P NMR ($CDCl_3$) δ −31,74.

2-(1′-Ferrocenyl)ethyl-3,4-dimethylphosphacymantrene, 3. 2-(1′-Hydroxyethyl)-3,4-dimethylphosphacymantrene, **1** (330 mg, 1.12 mmol), and 186 mg of ferrocene (1 mmol) were placed in a Schlenk tube under nitrogen atmosphere, and 20 mL of distilled dichoromethane was added via a septum. The yellow solution was cooled to 0 °C, and 160 mg of aluminum chloride (1.2 mmol) was added. The solution turned

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(5) The transformation of phosphacymantrenes into phospholes is described in: Deschamps, B.; Toullec, P.; Ricard, L.; Mathey, F. *J. Organomet. Chem.* **2001**, *634*, 131.

(6) Laporte, F.; Mercier, F.; Ricard, L.; Mathey, F. *J. Am. Chem. Soc.* **1994**, *116*, 3306. Deschamps, E.; Ricard, L.; Mathey, F. *J. Chem. Soc., Chem. Commun.* **1995**, 1561.

dark brown after 15 mn. The consumption of the starting phosphacymantrene was monitored by ^{31}P NMR spectroscopy after 2 h of reaction. The reaction medium was diluted by 50 mL of dichloromethane, and the solution was hydrolyzed using 100 mL of a saturated sodium hydrogen carbonate aqueous solution and washed with 100 mL of brine. The organic layer was collected and dried with magnesium sulfate, and the solvents were removed under vacuum to give the crude products as an orange oil. Chromatography over silica gel was carried out with a 90:10 hexane/ether mixture as the eluent. The two diastereoisomers **3a** and **3b** of the final product (180 mg) were isolated as a mixture (80:20): 40% yield; MS *m*/*z* 463 (M^+, 39), 378 ($M^+ - 3CO + 1$, 100), 312 ($M^+ - 3CO - C_5H_5$, 9), 258 ($M^+ - 3CO - C_5H_5 - Mn$, 36); HRMS for the mixture **3a**+**3b** calcd 461.9880, found 461.9880.

3a: ^{1}H NMR ($CDCl_3$) δ 1.50 (d, $^4J_{H-P} = 7$ Hz, 3H, benzylic CH_3), 1.99 (s, 3H, C_β-CH_3), 2.07 (s, 3H, C_β-CH_3), 3.20 (m, 1H, benzylic proton), 4.1−4.25 (m, 9H, Cp et Cp′); {^{1}H}^{13}C NMR ($CDCl_3$) δ 13.76 (s, C_β-CH_3), 16.55 (s, C_β-CH_3), 24.28 (d, $^3J_{C-P} = 13$ Hz, benzylic CH$_3$), 33.10 (d, $^2J_{C-P} = 15$ Hz, benzylic *C*), 66.90 (s, Cp), 67.72 (s, Cp), 67.89 (s, Cp), 69.28 (s, Cp), 90.31 (d, $^1J_{C-P} = 59$ Hz, C^5), 110.23 (d, $^2J_{C-P} = 6$ Hz, C^4), 113.99 (d, $^2J_{C-P} = 7$ Hz, C^3), 128.15 (d, $^1J_{C-P} = 63$ Hz, C^2), 225.18 (s, *C*O); {^{1}H}^{31}P NMR ($CDCl_3$) δ −35.10.

3b: ^{1}H NMR ($CDCl_3$) δ 1.45 (d, $^4J_{H-P} = 7$ Hz, 3H, benzylic CH_3), 2.05 (s, 3H, C_β-CH_3), 2.10 (s, 3H, C_β-CH_3); {^{1}H}^{13}C NMR ($CDCl_3$) δ 13.53 (s, C_β-CH_3), 16.46 (s, C_β-CH_3), 23.35 (m, benzylic CH$_3$), 34.58 (d, $^2J_{C-P} = 15$ Hz, benzylic *C*), 67.17 (d, $J = 6$ Hz, Cp), 67.68 (s, Cp), 68.34 (s, Cp), 69.16 (s, Cp), 88.74 (d, $^1J_{C-P} = 60$ Hz, $C^{5'}$), 109.76 (d, $^2J_{C-P} = 6$ Hz, $C^{4'}$), 114.84 (d, $^2J_{C-P} = 6$ Hz, $C^{3'}$), 130.16 (d, $^1J_{C-P} = 62$ Hz, $C^{2'}$), 225.18 (s, *C*O); {^{1}H}^{31}P NMR ($CDCl_3$) δ −28.80.

1,3-Dimethoxy-4,6-bis[1′-(3″,4″-dimethylphosphacymantrenyl)ethyl]benzene, 4. 2-(1′-Hydroxyethyl)-3,4-dimethylphosphacymantrene, **1** (620 mg, 2.1 mmol), and 140 mg of 1,3-dimethoxybenzene (1 mmol) were placed in a Schlenk tube under nitrogen atmosphere, and 20 mL of distilled dichoromethane was added via a septum. The yellow solution was cooled to 0°C and 300 mg of aluminum chloride (2.24 mmol) were added. The solution turned dark brown after 15 mn. The consumption of the starting phosphacymantrene was monitored by ^{31}P NMR spectroscopy after 2 h of reaction. The reaction medium was diluted by 50 mL of dichloromethane, the solution was hydrolyzed using 100 mL of a saturated sodium hydrogen carbonate aqueous solution and washed with 100 mL of brine. The organic layer was collected and dried with magnesium sulfate, and the solvents were removed under vacuum to give the crude products as a yellow oil. A first chromatography over silica gel was carried out with a 90:10 hexane/ether mixture as the eluent. A mixture of isomers of the final product (480 mg) was isolated in 70% total yield. A second chromatography over silica gel carried out with the same eluent mixture led to the isolation of 80 mg of the isomer **4a** and 100 mg of the isomer **4b** as yellow solids.

4a: ^{1}H NMR ($CDCl_3$) δ 1.27 (dd, $^4J_{H-P} = 7$ Hz, 6H, benzylic CH_3), 1.71 (s, 6H, $C^{3''}$-CH_3), 2.12 (s, 6H, $C^{4''}$-CH_3), 3.75 (m, 2H, benzylic proton), 3.82 (s, 6H, CH_3-O), 4.24 (d, $^2J_{H-P} = 36$ Hz, 2H, $C^{5''}$-*H*), 6.34 (s, 1H, C^2-*H*), 6.74 (s, 1H, C^5-*H*); {^{1}H}^{13}C NMR ($CDCl_3$) δ 12.46 (s, $C^{3''}$-CH_3), 15.70 (s, $C^{4''}$-CH_3), 22.24 (d, $^3J_{C-P} = 17$ Hz, benzylic CH$_3$), 33.07 (d, $^2J_{C-P} = 13$ Hz, benzylic *C*), 55.32 (s, CH$_3$-O), 90.62 (d, $^1J_{C-P} = 60$ Hz, $C^{5''}$), 94.46 (s, C^2), 109.24 (d, $^2J_{C-P} = 5$ Hz, $C^{4''}$), 113.92 (d, $^2J_{C-P} = 7$ Hz, $C^{3''}$), 127.00 (s, C^5), 127.90 (d, $^1J_{C-P} = 63$ Hz, $C^{2''}$), 155.28 (s, C^1, C^3), 224.42 (s, *C*O); {^{1}H}^{31}P NMR (CH_2Cl_2) δ −39.95; HRMS for **4a** calcd 690.0177, found 690.0182.

4b: ^{1}H NMR ($CDCl_3$) δ 1.32 (dd, $^4J_{H-P} = 6$ Hz, 6H, benzylic CH_3), 1.59 (s, 6H, $C^{3''}$-CH_3), 2.06 (s, 6H, $C^{4''}$-CH_3), 3.83 (m, 2H, benzylic proton), 3.85 (s, 6H, CH_3-O), 4.23 (d, $^2J_{H-P} = 35$ Hz, 2H, $C^{5''}$-*H*), 6.36 (s, C^2-*H*), 6.73 (s, C^5-*H*); {^{1}H}^{13}C NMR ($CDCl_3$) δ 12.30 (s), 15.65 (s), 22.18 (d, $^3J_{C-P} = 17$ Hz, benzylic CH$_3$), 32.32 (d, $^2J_{C-P} = 14$ Hz, benzylic *C*), 55.44 (s, CH$_3$-O), 90.83 (d, $^1J_{C-P} = 60$ Hz, $C^{5''}$), 94.14 (s, C^2), 109.13 (d, $^2J_{C-P} = 7$ Hz, $C^{4''}$), 113.20 (d, $^2J_{C-P} = 7$ Hz, $C^{3''}$), 125.48 (s, C^5), 126.54 (s, C^4), 128.47 (d, $^1J_{C-P} = 64$ Hz, $C^{2''}$) 155.05 (s, C^1, C^3), 224.30 (s, *C*O); {^{1}H}^{31}P NMR (CH_2Cl_2) δ −40.79. MS *m*/*z* 691 ($M^+ + 1$, 4), 606 ($M^+ - 3CO$, 53), 522 ($M^+ - 6CO$, 100), 467 ($M^+ - 6CO - Mn$, 25); HRMS for **4b** calcd 690.0177, found 690.0182.

Crystallographic data for $C_{30}H_{30}Mn_2O_8P_2$ (**4b**): $M = 690.36$ g/mol; triclinic; space group $P\bar{1}$; $a = 9.383(5)$ Å, $b = 12.956(5)$ Å, $c = 14.152(5)$ Å, $\alpha = 67.370(5)°$, $\beta = 71.510(5)°$, $\gamma = 82.330(5)°$, $V = 1505.8(11)$ Å^3; $Z = 2$; $D = 1.523$ g cm^{-3}; $\mu = 0.994$ cm^{-1}; $F(000) = 708$. Crystal dimensions 0.20 × 0.14 × 0.10 mm. Total reflections collected 13 387 and 6947 with $I > 2\sigma(I)$. Goodness of fit on F^2 1.047; $R(I>2\sigma(I)) = 0.0362$, wR2 = 0.0902(all data); maximum/minimum residual density 0.404(0.063)/−0.502(0.063) e Å^{-3}. Data were collected on a KappaCCD diffractometer at 150.0(1) K with Mo Kα radiation ($\lambda = 0.71073$ Å). Full details of the crystallographic analysis are described in the Supporting Information.

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Supporting Information Available: Crystallographic data for **4b** and {^{1}H}^{13}C NMR spectra of **2a**+**b**, **3a**+**b**, and **4b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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