Notes

Synthesis and Highly Diastereoselective Palladation of (η^5-(*S*)-2-(4-Methylethyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt

Andrew M. Stevens and Christopher J. Richards*,‡

Department of Chemistry, Cardiff University, P.O. Box 912, Cardiff, CF1 3TB, U.K.

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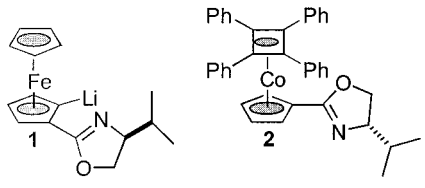
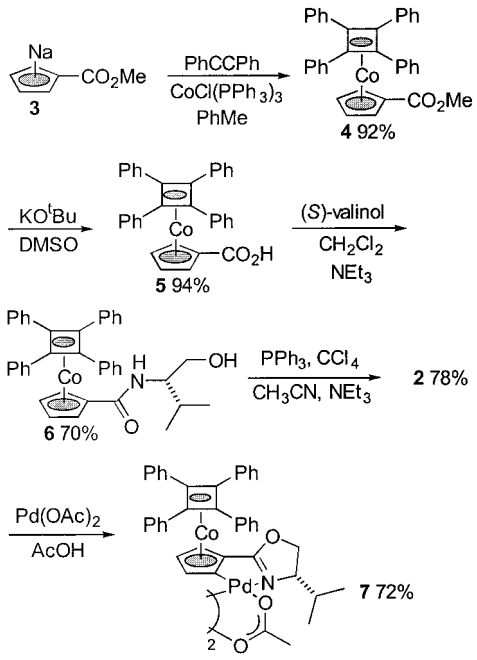
Summary: Starting from sodium carbomethoxycyclopentadienide, diphenylacetylene, and chlorotris(triphenylphosphine)cobalt(I), the title compound was obtained in four steps and 47% overall yield. On reaction with $Pd(OAc)_2$, a single cyclopalladated diastereoisomer of (S)-($_p$R) configuration was isolated in 72% yield.

Introduction

Interest in the planar chirality displayed by differently substituted 1,2-cyclopentadienyl ligands attached to a metal has resulted in a number of methods for the asymmetric synthesis of ferrocene[1] and cymantrene complexes.[2] Many of these involve diastereoselective ortho-lithiation mediated by a suitable group such as the oxazoline auxiliary. When attached to ferrocene, this controls the selective formation of **1**, in which the oxazoline isopropyl substituent is oriented toward the unsubstituted cyclopentadienyl ring.[3] As part of a program investigating derivatives of (η^5-C_5H_5)(η^4-C_4Ph_4)-Co complexes as components of molecular gearing devices,[4] we wished to develop a method for the diastereoselective ortho-metalation of the corresponding oxazoline derivative **2**. In this paper we describe the synthesis and palladation of this complex and report on the effect of the four phenyl substituents on the selectivity and orientation of this metalation.



Scheme 1



Results and Discussion

The carbomethoxy-substituted complex **4** has previously been synthesized in 52% overall yield from **3** via the intermediate cobalt dicarbonyl adduct.[5] To avoid the use of metal carbonyls, diphenylacetylene was combined directly with **3** and $CoCl(PPh_3)_3$ to give a 92% yield of ester **4**.[6] Subsequent hydrolysis with potassium *tert*-butoxide in DMSO gave an excellent yield of the required acid, from which the corresponding acid chloride was generated in situ with oxalyl chloride. On addition of (*S*)-valinol this yielded the β-hydroxy amide **6**, which was dehydrated under Appel conditions[7] to give oxazoline **2** in 47% overall yield for the four steps (Scheme 1).

‡ RichardsCJ@cardiff.ac.uk. Fax: +44 1222 874030.

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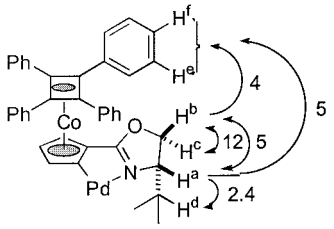

Figure 1. NOE connectivity and percentage enhancements for **7**.

Attempts to effect diastereoselective lithiation of **2** with BuLi, *sec*-BuLi, and *tert*-BuLi all failed to result in incorporation of lithium into the molecule, despite prolonged reaction times and the use of additives such as TMEDA. As a consequence, our attention turned to palladation, prompted by previous reports on the ortho-palladation of (η^5-$C_5H_4CH_2N(CH_3)_2$)(η^4-C_4Ph_4)Co[8] and 2-aryloxazolines.[9] Accordingly, palladium acetate and oxazoline **2** were heated at 95 °C in glacial acetic acid for 30 min, and on cooling an orange crystalline solid was isolated by filtration. Examination of the ^{1}H NMR of this material revealed the presence of only three cyclopentadienyl proton signals, and that palladation had occurred ortho to the oxazoline was confirmed by the doublet/triplet/doublet coupling pattern arising from these three adjacent hydrogens. Of greater significance was the presence of only one set of signals in this and all other regions of the spectra, revealing that a single diastereoisomer had been isolated. The single peak observed for the acetate methyl groups reveals that the two palladated oxazolines adopt an anti relationship about these bridging ligands.[10] Examination of the concentrated mother liquors revealed that none of the product remained in this residue, nor did the ^{1}H NMR spectrum of this material indicate the presence of other possible diastereomeric acetate dimers.

The orientation of this diastereoselective palladation was determined by NOE difference spectroscopy (Figure 1). Irradiation of H^a (3.00 ppm) gave a 5% enhancement of the triplet at 3.38 ppm, confirming this as arising from H^b. The H^a irradiation also gave rise to a 5% enhancement of the overlapping signals corresponding to the meta/para hydrogens of the four phenyl groups, and an enhancement of similar magnitude was observed on irradiation of H^b. Significantly, no such enhancement was found on irradiation of H^c (4.08 ppm) or of either of the two diastereotopic methyl doublets (0.02 and 0.47 ppm). That H^a and H^b are in the vicinity of the "roof" defined by the four phenyl groups, as was initially suspected by the rather low chemical shift of these two signals, confirms the new element of planar chirality as $_pR$.

Previously reported methods for the diastereoselective ortho-palladation of substituted metallocenes have generally resulted in incomplete stereochemical control,[11] and only recently were the first fully selective examples described.[12] Furthermore, the conditions used in all of these previous palladations (Na_2PdCl_4/AcOH/MeOH at room temperature) are in stark contrast to the more vigorous conditions used in this work. Both the high selectivity observed and the opposite orientation of this metalation compared to that previously found for ferrocenyloxazolines are rationalized through the inability of complex **2** to access rotamer A (Figure 2). This would result in a severe repulsive interaction between the oxazoline isopropyl substituent and the phenyl "roof", an effect avoided with rotamer B. This restriction of **2** to a single rotamer results in the oxazoline substituent displaying *effective* planar chirality, as if it were directly bonded to a second position of the cyclopentadienyl ring. The implications of this arrangement and the use of such complexes in asymmetric catalysis are currently under investigation.

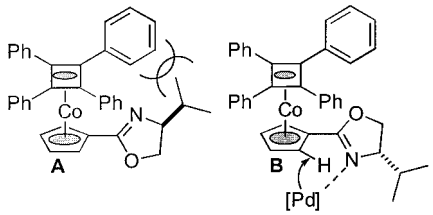

Figure 2. Origin of diastereoselective palladation.

Experimental Section

Tetrahydrofuran was distilled from sodium benzophenone ketyl, and toluene, dichloromethane, and acetonitrile were distilled from calcium hydride. Petroleum ether refers to that fraction boiling in the range 40−60 °C. Column chromatography was performed on Matrix silica 60 (35−70 μm). All reactions, with the exception of the palladation, were performed under a nitrogen atmosphere.

(η^5-Carbomethoxycyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt. 4. To a solution of chlorotris(triphenylphosphine)cobalt(I)[13] (7.24 g, 8.2 mmol) and diphenylacetylene (3.36 g, 18.9 mmol) in toluene (56 mL) was added a solution of sodium carbomethoxycyclopentadienide (**3**)[14] (1.38, 9.4 mmol) in THF (14 mL). The resulting mixture was heated at reflux for 5 h and then allowed to cool to room temperature. The solvent was removed in vacuo and the residue suspended in petroleum ether (50 mL) and collected by filtration to give **4** as a yellow crystalline solid (4.06 g, 92%): mp 222 °C (EtOAc/petroleum ether) [lit.[5] 219−221 °C]; δ_H (400 MHz, $CDCl_3$) 3.24 (3 H, s, $-CH_3$), 4.84 (2 H, brs, Cp*H*), 5.27 (2 H, brs, Cp*H*), 7.22−7.32 (12 H, m, *m*+*p*-Ph*H*), 7.42−7.48 (8 H, m, *o*-Ph*H*); δ_C {^{1}H} (100 MHz, $CDCl_3$) 51.6 ($-CH_3$), 76.4 (C_4Ph_4), 84.9 (Cp*C*), 86.8 (Cp*C*), 87.1 (*ipso*-Cp*C*), 127.1 (*p*-Ph*C*), 128.3 (Ph*C*), 129.2 (Ph*C*), 135.5 (*ipso*-Ph*C*), 167.0 ($-CO_2CH_3$).

(η^5-Carboxycyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt, 5. A mixture of **4** (0.210 g, 0.39 mmol) and potassium *tert*-butoxide (0.66 g, 5.9 mmol) in DMSO (6 mL) was stirred at room temperature for 15 h and then quenched with 2 M HCl (5 mL). After extraction with EtOAc (80 mL), the organic phase was separated and dried ($MgSO_4$) and the

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solvent removed in vacuo. The residue was column chromatographed (20% EtOAc/petroleum ether) to give **5** as an orange crystalline solid (0.192, 94%): mp 240−244 °C (EtOAc) [lit.[5] 246−248 °C]; δ_H (400 MHz, $CDCl_3$) 4.78 (2 H, brs, Cp*H*), 5.22 (2 H, brs, Cp*H*), 7.21−7.24 (12 H, m, *m*+*p*-Ph*H*), 7.43−7.47 (8 H, m, *o*-Ph*H*); δ_C {^{1}H} (100 MHz, $CDCl_3$) 77.2 (C_4Ph_4), 89.1 (Cp*C*), 89.3 (Cp*C*), 92.9 (*ipso*-Cp*C*), 127.7 (*p*-Ph*C*), 128.8 (Ph*C*), 129.0 (Ph*C*), 135.0 (*ipso*-Ph*C*), 191.1 (−*C*O$_2$H).

(η^5-(*S*)-*N*-2-(1-Hydroxy-3-methylbutyl)carboxamidecyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt, 6. To a solution of **5** (0.163 g, 0.31 mmol) in CH_2Cl_2 (2 mL) was added oxalyl chloride (0.06 mL, 0.7 mmol), and the resulting red solution was stirred at room temperature for 20 min. The solvent and excess oxalyl chloride were removed in vacuo, and the crude acid chloride was dissolved in CH_2Cl_2 (2 mL) and added to a solution of (*S*)-valinol (0.043 g, 0.42 mmol) in triethylamine (0.1 mL) and CH_2Cl_2 (1 mL). The resulting orange reaction mixture was stirred at room temperature overnight, quenched with water (6 mL), and extracted with EtOAc (3 × 15 mL). The combined organic phases were dried ($MgSO_4$) and evaporated in vacuo, and the residue was column chromatographed (3% MeOH/CH_2Cl_2) to give **6** as an orange crystalline solid (0.133 g, 70%): mp 214−217 °C (EtOAc/petroleum ether); $[\alpha]_D^{24} = -16.9$ (*c* 0.125, $CHCl_3$); (found C, 76.83; H, 5.82; N, 2.21; $C_{39}H_{36}CoNO_2$ requires C, 76.83; H, 5.95; N, 2.30); ν_{max}/cm^{-1} 3364 (OH), 1666 (C═O); δ_H (400 MHz, $CDCl_3$) 0.85 (3 H, d, *J* 6.7, −C*H*$_3$), 0.94 (3 H, d, *J* 6.7, −C*H*$_3$), 1.59 (1 H, oct, *J* 6.7, −C*H*(CH$_3$)$_2$), 3.17 (1 H, brs, O*H*), 3.27−3.42 (3 H, m, −C*H*C*H*$_2$OH), 4.70 (1 H, brs, Cp*H*), 4.74 (1 H, brs, Cp*H*), 4.97 (1 H, brs, Cp*H*), 5.11 (1 H, brs, Cp*H*), 5.35 (1 H, d, *J* 6.7, N*H*), 7.26−7.32 (12 H, m, *m*+*p*-Ph*H*), 7.46−7.49 (8 H, m, *o*-Ph*H*); δ_C {^{1}H} (100 MHz, $CDCl_3$) 19.6 (2 × −*C*H$_3$), 29.4 (−*C*H(CH$_3$)$_2$), 59.0 (−*C*HCH$_2$−), 64.6 (−*C*H$_2$OH), 76.7 (C_4Ph_4), 82.5 (Cp*C*), 82.6 (Cp*C*), 87.0 (Cp*C*), 87.4 (Cp*C*), 91.0 (*ipso*-Cp*C*), 127.3 (*p*-Ph*C*), 128.6 (Ph*C*), 129.2 (Ph*C*), 135.6 (*ipso*-Ph*C*), 167.0 (*C*═O); *m*/*z* (EI) 609 (M$^+$, 100), 591 (27), 523 (11), 479 (4), 415 (30), 356 (8), 178 (94).

(η^5-(*S*)-2-(4-Methylethyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt, 2. To a solution of **6** (0.113 g, 0.19 mmol) and triphenylphosphine (0.210 g, 0.80 mmol) in triethylamine (0.13 mL, 0.9 mmol) and acetonitrile (25 mL) was added CCl_4 (0.18 mL, 1.9 mmol) and the resultant mixture stirred at room temperature for 15 h. After quenching with water (20 mL), the mixture was extracted with petroleum ether (5 × 60 mL), and after separation, the organic phase was dried ($MgSO_4$) and filtered and the solvent removed in vacuo. The residue was column chromatographed (10% EtOAc/petroleum ether) to give **2** as an orange crystalline solid (0.085 g, 78%): mp 160−162 °C (EtOAc/petroleum ether); $[\alpha]_D^{24} = -55.2$ (*c* 0.09, $CHCl_3$); (found C, 78.99; H, 5.92; N, 2.23; $C_{39}H_{34}$-CoNO requires C, 79.17; H, 5.79; N, 2.37); ν_{max}/cm^{-1} 1654 (C═N); δ_H (400 MHz, $CDCl_3$) 0.77 (3 H, d, *J* 6.7, −C*H*$_3$), 0.97 (3 H, d, *J* 6.7, −C*H*$_3$), 1.40 (1 H, oct, *J* 6.7, −C*H*(CH$_3$)$_2$), 3.41−3.56 (3 H, m, −C*H*C*H*$_2$−), 4.62 (1 H, brs, Cp*H*), 4.80 (1 H, brs, Cp*H*), 5.09 (1 H, brs, Cp*H*), 5.20 (1 H, brs, Cp*H*), 7.17−7.27 (12 H, m, *m*+*p*-Ph*H*), 7.44−7.47 (8 H, m, *o*-Ph*H*); δ_C {^{1}H} (100 MHz, $CDCl_3$) 20.4 (−*C*H$_3$), 21.6 (−*C*H$_3$), 35.0 (−*C*H(CH$_3$)$_2$), 71.5 (−*C*HCH$_2$−), 74.7 (−CH*C*H$_2$−), 78.0 (C_4Ph_4), 84.1 (*ipso*-Cp*C*), 86.4 (Cp*C*), 87.0 (Cp*C*), 87.1 (Cp*C*), 88.4 (Cp*C*), 126.8 (*p*-Ph*C*), 128.3 (Ph*C*), 129.3 (Ph*C*), 135.8 (*ipso*-Ph*C*), 162.6 (*C*═N); *m*/*z* (EI) 591 (M$^+$, 100), 415 (82), 356 (8), 178 (60).

Di-μ-acetatobis[(η^5-(*S*)-($_p$*R*)-2-(2′-(4′-methylethyl)oxazolinyl)cyclopentadienyl, 1-*C*, 3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium, 7. A solution of **2** (0.314 g, 0.53 mmol) and $Pd(OAc)_2$ (0.119 g, 0.53 mmol) in glacial acetic acid (1 mL) was heated for 30 min at a temperature of 95 °C. After the resultant orange mixture had cooled to room temperature, it was diluted with cold glacial acetic acid (1 mL), and the product was isolated by filtration and washed with further glacial acetic acid (1 mL). After drying in vacuo, complex **7** was obtained as an orange crystalline solid (0.290 g, 72%): mp 189−194 °C; $[\alpha]_D^{24} = +942$ (*c* 0.215, $CHCl_3$); (found C, 65.21; H, 5.01; N, 1.56; $C_{82}H_{72}Co_2N_2O_6Pd_2$ requires C, 65.13; H, 4.80, N, 1.85); ν_{max}/cm^{-1} 1591 (C═N), 1498, 1408 (acetate bridge); δ_H (400 MHz, $CDCl_3$) 0.02 (6 H, d, *J* 7.2, −C*H*$_3$), 0.47 (6 H, d, *J* 7.2, −C*H*$_3$), 1.75−1.79 (2 H, m, −C*H*(CH$_3$)$_2$), 1.95 (6 H, s, CO$_2$C*H*$_3$), 2.99−3.01 (2 H, m, −C*H*CH$_2$−), 3.38 (2 H, t, *J* 9.0, −C*H*H−), 4.08 (2 H, dd, *J* 8.5, 4.0, −CH*H*−), 4.23 (2 H, t, *J* 2.4, Cp*H*), 4.62 (2 H, d, *J* 1.6, Cp*H*), 4.69 (2 H, d, *J* 2.3, Cp*H*), 7.21−7.29 (24 H, m, *m*+*p*-Ph*H*), 7.65−7.67 (16 H, m, *o*-Ph*H*); δ_C {^{1}H} (100 MHz, $CDCl_3$) 13.5 (−*C*H$_3$), 19.0 (−*C*H$_3$), 24.3 (−*C*H(CH$_3$)$_2$), 29.3 (*C*H$_3$CO$_2$), 65.3 (−*C*HCH$_2$−), 71.4 (−CH*C*H$_2$−), 71.4 (C_4Ph_4), 79.6 (*ipso*-Cp*C*CN), 85.1 (Cp*C*), 85.6 (Cp*C*), 87.0 (Cp*C*), 98.3 (*ipso*-Cp*C*Pd), 126.4 (*p*-Ph*C*), 128.3 (Ph*C*), 129.7 (Ph*C*), 136.3 (*ipso*-Ph*C*), 171.0 (*C*═N), 181.2 (*C*O$_2$); *m*/*z* (APCI) 1512 (M$^+$ 18), 551 (100).

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