Preparation and Structural Features of Lithium Cyclopentadienides that Contain Amino Acid-Derived Cp-Substituents

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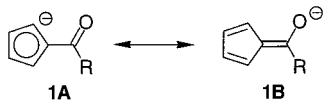
*Summary: Treatment of N-protected amino acid active esters, e.g., **3**, formed by the reaction of N,N-dibenzylalanine (**2**) with DCC and hydroxybenztriazole, with 2 molar equiv of CpLi gives the corresponding amino acid-substituted Cp-anion equivalents (e.g., **4**). The X-ray crystal structure analysis of **4** has revealed a dimeric pentafulvenolate-type structure. Reaction of $FeCl_2$ or $(PPh_3)_3RuCl_2$ with compound **4** and related reagents yields the respective 1,1′-difunctionalized metallocenes (**7**, **8**).*

Introduction

Acyl-functionalized cyclopentadienyl anion equivalents and related systems are becoming of increasing interest as reagents in organometallic synthesis.[1] The acyl cyclopentadienides can principally be regarded as resonance hybrids of functionalized cyclopentadienyl anion (**1A**) and oxy-anion-substituted pentafulvene descriptions (**1B**), and as such they seem to behave structurally. [Acetyl-C_5H_4 sodium]·THF (**1a**, R = CH_3) may serve as a typical example: In the crystal it exhibits dimeric structural subunits that contain O_2Na_2 four-membered rings, and each of these is connected by intermolecular electrostatic η^5-Cp−Na contacts [with Na−C(Cp) distances ranging between 2.69(1) and 2.94(1) Å][2] to form an indefinitely extending columnar structural array in the crystal.[3] We here describe a novel synthetic pathway to a related amino acid-functionalized cyclopentadienyllithium reagent where the structural characterization has revealed a marked structural change caused by the presence of the newly introduced amino substituent serving as an internal donor ligand that disrupts the otherwise observed alkali metal−Cp interaction.

Chart 1



1A 1B

Results and Discussion

For the preparation of the amino acid-functionalized cyclopentadienides we have adopted a commonly used coupling method from peptide chemistry.[4] In a typical example *N*,*N*-dibenzylalanine (**2**) was converted to the active ester (**3**) by treatment with hydroxybenztriazole (HOBt) and dicyclohexylcarbodiimide (DCC) in dichloromethane. The resulting reagent (**3**) was then reacted with 2 molar equiv of cyclopentadienyllithium in THF, one of which attacks the activated alanine carbonyl group to form the new carbon−carbon bond, and the other is used as a base in the subsequent deprotonation step. The amino acid-functionalized cyclopentadienyllithium system (**4**, $[\alpha]_D^{20} = -115°$) was isolated as a pale yellow solid in 85% yield using this procedure.

The method was also used to attach the N-protected Ala-substituent at the 1-position of the indenyl ligand (for details see the Supporting Information). Other amino acids, containing other N-protecting groups, couple equally well, as shown by the *Z*-Pro-CpLi example depicted in Scheme 1 (**6**, 74% isolated, $[\alpha]_D^{20} = -154°$).

In THF-d_8 solution compound **4**, which then probably is present as a C_5H_4[COLi(THF)$_3$]CHMeNBz$_2$ THF solvate, exhibits four separate ^{1}H NMR resonances of the five-membered ring methine protons at δ 6.47, 6.09 (α-CH) and 5.92, 5.77 (β-CH) [with corresponding ^{13}C NMR signals at δ 118.1, 113.6/117.6, 115.2], which indicates hindered rotation about the exocyclic C1−C6 partial double bond at ambient temperature and thus the presence of a fulvenoid character [^{13}C NMR: δ (C1): 125.6, δ (C2): 185.1].[5]

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† X-ray crystal structure analysis.

(1) (a) Review: Macomber, D. W.; Hart, W. P.; Rausch, M. D. *Adv. Organomet. Chem.* **1982**, *21*, 1−55. (b) Selected examples: Arthurs, M.; Al-Daffaee, H. K.; Haslop, J.; Kubal, G.; Pearson, M. D.; Thatcher, P.; Curzon, E. *J. Chem. Soc., Dalton Trans.* **1987**, 2615−2619. Bitterwolf, T. E.; Hubler, T. L.; Rheingold, A. L. *J. Organomet. Chem.* **1992**, *431*, 199−214. Jones, S. S.; Rausch, M. D.; Bitterwolf, T. E. *J. Organomet. Chem.* **1993**, *450*, 27−31. Blais, M. S.; Rausch, M. D. *Organometallics* **1994**, *13*, 3557−3563. Etkin, N.; Ong, C. M.; Stephan, D. W. *Organometallics* **1998**, *17*, 3656−3660. Klass, K.; Duda, L.; Kleigrewe, N.; Erker, G.; Fröhlich, R.; Wegelius, E. *Eur. J. Inorg. Chem.* **1999**, 11−19. Klass, K.; Fröhlich, R.; Erker, G. *J. Chem. Soc., Dalton Trans.* **1999**, 4457−4461. Flores, J. C.; Hernández, R.; Royo, P.; Butt, A.; Spaniol, T. P.; Okuda, J. *J. Organomet. Chem.* **2000**, *593−594*, 202−210.

(2) Rogers, R.; Atwood, J. L.; Rausch, M. D.; Macomber, D. W.; Hart, W. P. *J. Organomet. Chem.* **1982**, *238*, 79−85. The bond lengths (Å) inside the Cp−C(O)Me$^-$ unit of **1a** are as follows: 1.26(1) (C6−O1), 1.41(1) (C6−C1), 1.43(1) (C1−C2), 1.44(1) (C1−C5), 1.39(1) (C2−C3), 1.41(1) (C3−C4), 1.35(1) (C4−C5).

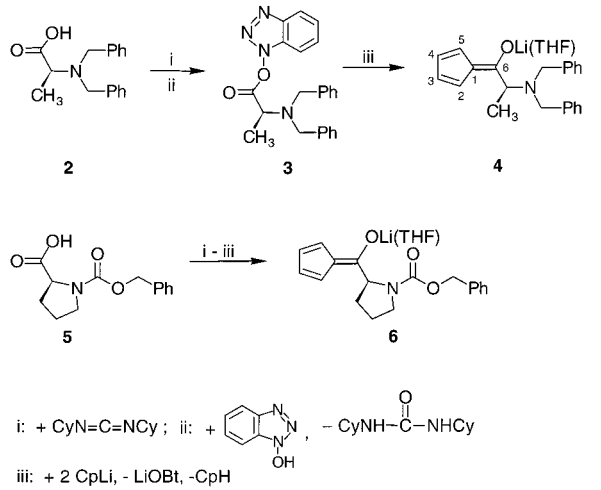
(3) Jutzi, P. *J. Organomet. Chem.* **1990**, *400*, 1−17. Jutzi, P.; Burford, N. *Chem. Rev.* **1999**, *99*, 969−990, and references therein.

(4) Jakubke, H.-D. *Peptide*; Spektrum-Verlag: Heidelberg, 1996. Bodanszky, M. *Principles of Peptide Synthesis*, 2nd ed.; Springer-Verlag: Berlin, Heidelberg, 1993, and references therein.

(5) The rotational barrier about the C6−C1 bond in the heteroatom-stabilized system (6-dimethylamino)pentafulvene was determined at $\Delta G^{\ddagger}_{rot} = 22.1$ kcal mol^{-1}: Downing, A. P.; Ollis, W. D.; Sutherland, I. O. *J. Chem. Soc. B* **1969**, 111−119.

10.1021/om000778t CCC: $20.00
Publication on Web 01/06/2001

Scheme 1



Single crystals of **4** suited for an X-ray crystal structure analysis were obtained by diffusion of pentane vapor into a solution in toluene. In the crystal compound **4** is present as a dimer that contains one molecule of THF coordinated to each lithium atom. The central unit of the dimer comprises a distorted square arrangement of two lithium atoms and two fulvenolate oxygens [Li–O distances between 1.908(7) and 1.966(7) Å, angles between 88.1(3)° and 91.2(3)°]. The four-membered ring is slightly puckered [θ Li1A–O1A–Li1B–O1B: 12.5(3)°]. Two heterocyclic five-membered rings are found annelated in an idealized (but not crystallographical) C_2-symmetric arrangement (see Figure 1). The connecting Li–N linkages are rather long at 2.431(7) Å (Li1A–N1A) and 2.147(6) Å (Li1B–N1B), and the individual annelated five-membered rings are markedly distorted from planarity [e.g., θ O1A–Li1A–N1A–C7A: −30.5(2)°]. Coordinated THF completes the strongly distorted pseudo-tetrahedral κ^3O,κN-arrangement of ligands around each lithium atom inside the tricyclic dimetallic dimer units of **4** [Li1A–O31A: 1.972(6) Å, Li1B–O31B: 1.934(7) Å]. The fulvenolate C6A–O1A bond length in **4** amounts to 1.291(4) Å [C6B–O1B: 1.279(4) Å]. The exocyclic C1A–C6A bond length is 1.381(5) Å [C1B–C6B: 1.405(5) Å], and the π-system in the connected C_5H_4 ring is markedly alternating [e.g., C2A–C3A: 1.364(5) Å, C3A–C4A: 1.432(6) Å, C4A–C5A: 1.363(5) Å]. These values are close to typical values found in pentafulvenes that contain heteroatom-donor substituents at their exocyclic C6 position.[6,7] However, the small systematic deviations (e.g., of the C6–O1 or C1–C6 bond lengths) from standard values probably indicate some additional π-delocalization within the cross-conjugated C1 to C6(O1) framework. We conclude that compound **4** is stabilized by internal nitrogen–lithium bonding at the expense of a possible (electrostatic) Cp–Li interaction. The bonding features of the $C_5H_4C(O)R^-$ unit correspond to a dominant fulvenolate character (resonance form **B** in Chart 1)

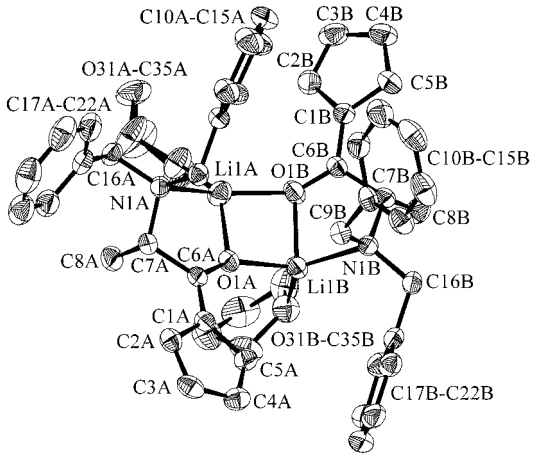
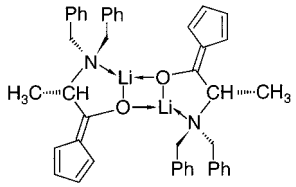
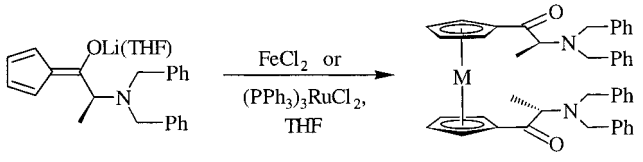


Figure 1. Structure of the dimeric subunit of **4** in the crystal. Selected bond lengths (Å) and angles (deg): Li1A–O1A 1.908(7), O1B–Li1A 1.958(7), O1A–Li1B 1.910(6), O1B–Li1B 1.966(7), C1A–C2A 1.444(5), C1A–C5A 1.442(5), C1B–C2B 1.432(5), C1B–C5B 1.433(5), C2B–C3B 1.375(6), C3B–C4B 1.426(6), C4B–C5B 1.367(6); N1A–Li1A–O1B 141.1(3), N1B–Li1B–O1A 124.5(3), O1A–Li1A–O31A 136.5(4), O1B–Li1B–O31B 110.1(3), O1A–Li1B–O31B 104.2(3), O1B–Li1A–O31A 111.1(3), N1A–Li1A–O31A 102.2(3), N1B–Li1B–O31B 130.2(3), C6A–O1A–Li1B 146.0(3), C6B–O1B–Li1A 144.1(3), C6A–O1A–Li1A 120.1(3), C6B–O1B–Li1B 115.7(3); for additional values see the text.

Scheme 2. Schematic Description of the Dimeric Structure of 4



Scheme 3



with a small contribution of structural Cp–C(O)R$^-$ character (depicted by form **A**). The amino acid-derived fulvenolate reagents **4** (and **6**) were used as functionalized Cp-anion reagents for the synthesis of amino acid-substituted metallocenes.[8] Thus, treatment of **4** with anhydrous $FeCl_2$ or with tris(triphenylphosphine)$RuCl_2$ in a 2:1 molar ratio gave the optically active 1,1′-difunctionalized ferrocene (**7**) or ruthenocene (**8**) prod-

(6) See for example: Böhme, R.; Burzlaft, H. *Chem. Ber.* **1974**, *107*, 832–837. Ammon, H. L. *Acta Crystallogr. B* **1974**, *30*, 1731–1738. Ammon, H. L.; Wheeler, G. L. *J. Am. Chem. Soc.* **1975**, *97*, 2326–2336. Legzdins, P.; Lumb, S. A.; Young, V. G. Jr. *Organometallics* **1998**, *17*, 854–871. Duda, L.; Erker, G.; Fröhlich, R.; Zippel, F. *Eur. J. Inorg. Chem.* **1998**, 1153–1162.

(7) See 6,6-dimethylfulvene for a comparison: Chiang, J. F.; Bauer, S. H. *J. Am. Chem. Soc.* **1970**, *92*, 261–265.

(8) Carlström, A.-S.; Freid, T. *J. Org. Chem.* **1990**, *55*, 4175–4180. Amiens, C.; Balavoine, G.; Guibe, F. *J. Organomet. Chem.* **1993**, *443*, 207–219. Gorfti, A.; Salmain, M.; Jaouen, G.; McGlinchey, M. J.; Bennouna, A.; Mousser, A. *Organometallics* **1996**, *15*, 142–151. Jackson, R. F. W.; Turner, D.; Block, M. H. *Synlett* **1996**, 862–864. Oberhoff, M.; Duda, L.; Karl, J.; Mohr, R.; Erker, G.; Fröhlich, R.; Grehl, M. *Organometallics* **1996**, *15*, 4005–4011. Kayser, B.; Polborn, K.; Steglich, W.; Beck, W. *Chem. Ber./Recl.* **1997**, *130*, 171–177. Wolff, J. M.; Sheldrick, W. S. *Chem. Ber./Recl.* **1997**, *130*, 981–988. Kraatz, H.-B.; Lusztyk, J.; Enright, G. D. *Inorg. Chem.* **1997**, *36*, 2400–2405. Related reviews: Jaouen, G.; Vessières, A.; Butler, I. S. *Acc. Chem. Res.* **1993**, *26*, 361–369. Severin, K.; Bergs, R.; Beck, W. *Angew. Chem.* **1998**, *110*, 1722–1743; *Angew. Chem., Int. Ed.* **1998**, *37*, 1634–1654.

ucts in good yield. The reagent **6** was used in ferrocene synthesis in a similar manner (for details see the Supporting Information).

Experimental Section

The preparation of **4** and **7** is described as typical examples. Syntheses and detailed characterization of all compounds investigated in this study are provided with the Supporting Information. All reactions with organometallic compounds were carried out under argon using Schlenk-type glassware or in a glovebox. Solvents, including deuterated solvents used for NMR spectroscopy, were dried and distilled prior to use. *N*,*N*-Dibenzylalanine was prepared as described in the literature.[9]

Preparation of 4. For the preparation of the active ester **3** dicyclohexylcarbodiimide (2.06 g, 10.0 mmol) was added to a suspension of *N*,*N*-dibenzylalanine (**2**, 2.69 g, 10.0 mmol) and hydroxybenztriazol ("HOBt", 1.35 g, 10.0 mmol) in 50 mL of dichloromethane at 0 °C. The mixture was stirred for 1 h at 0 °C, and then the precipitated dicyclohexylurea was removed by filtration. Solvent was removed in vacuo. The remaining active ester **3** was dissolved in THF (50 mL). At −40 °C a solution of 1.78 g (24.7 mmol) of cyclopentadienyllithium in 30 mL of THF was added. The mixture was allowed to warm to room temperature overnight with stirring. Solvent was removed in vacuo and the residue taken up in diethyl ether. A precipitate (LiOBt and excess CpLi) was removed by filtration and the filtrate evaporated to dryness in vacuo to yield 3.37 g (85%) of **4** as a pale yellow solid. Mp: 119 °C, >175 °C decomp (DSC). $[\alpha]_D^{20} = -115°$ (*c* 0.2, dichloromethane). ^{1}H NMR (400.1 MHz, THF-d_8, 300 K): δ 7.38 (m, 4 H, o-Ph), 7.19 (m, 4 H, m-Ph), 7.10 (m, 2 H, p-Ph), 6.47 and 6.09 (br s, each 1 H, 2-/5-H), 5.92 and 5.77 (br s, each 1 H, 3-/4-H), 4.16 (q, ^3J = 7.2 Hz, 1 H, −C*H*Me), 3.89 and 3.70 (AX, ^2J = 14.8 Hz, 2 H each, CH_2Ph), 1.30 (d, ^3J = 7.2 Hz, CH_3). ^{13}C NMR (100.6 MHz, THF-d_8, 300 K): δ 185.1 (C6), 142.9 (ipso-C of Ph), 129.8 (o-Ph), 128.7 (m-Ph), 127.1 (p-Ph), 125.6 (C1), 118.1 and 113.6 (C2/C5), 117.6 and 115.2 (C3/C4), 57.3 (*C*HMe), 55.7 (*C*H_2Ph), 17.7 (CH_3). Anal. Calcd for $C_{26}H_{30}NO_2Li$ (395.5): C, 78.97; H, 7.65; N, 3.54. Found: C, 78.72; H, 8.05; N, 3.28. X-ray crystal structure analysis of **4**: formula $C_{26}H_{30}NO_2Li$, M = 395.45, yellow crystal 0.40 × 0.20 × 0.15 mm, a = 11.682(1), b = 13.419(3), c = 27.833(3) Å, V = 4363.1(11) Å^3, ρ_{calc} = 1.204 g cm^{-3}, μ = 5.76 cm^{-1}, empirical absorption correction via ψ scan data (0.802 ≤ T ≤ 0.919), Z = 8, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 1.54178 Å, T = 223 K, $\omega/2\theta$ scans, 4957 reflections collected (+h, +k, +l), [(sin θ)/λ] = 0.62 Å^{-1}, 4957 independent and 3759 observed reflections [$I \geq 2\sigma(I)$], 580 refined parameters, R = 0.056, wR_2 = 0.140, max. residual electron density 0.23 (−0.25) e Å^{-3}, Flack parameter −0.3(3), positional disorder in the THF molecule A, refined with split position for the carbon atoms (0.58(2):0.42(2)), hydrogens calculated and refined as riding atoms.

Data set was collected with an Enraf-Nonius CAD4 diffractometer. Programs used: data collection EXPRESS (Nonius B.V., 1994), data reduction MolEN (K. Fair, Enraf-Nonius B.V., 1990), structure solution SHELXS-97 (G. M. Sheldrick, *Acta Crystallogr.* **1990**, *A46*, 467−473), structure refinement SHELXL-97 (G. M. Sheldrick, Universität Göttingen, 1997), graphics DIAMOND (K. Brandenburg, Universität Bonn, 1997) and SCHAKAL (E. Keller, Universität Freiburg, 1997).

Preparation of 6. From 2.72 g (10.9 mmol) of *N*-benzyloxycarbonyl-L-proline, 1.47 g (10.9 mmol) of hydroxybenztriazole, and 2.24 g (10.9 mmol) of dicyclohexylcarbodiimide the active ester was generated analogously as described for compound **4**. The active ester **5** was dissolved in 70 mL of tetrahydrofuran and cooled to −78 °C, and a precooled solution of 1.57 g (21.8 mmol) of cyclopentadienyllithium in 30 mL of tetrahydrofuran was added. The yellow mixture was stirred overnight and allowed to warm to room temperature, resulting in a green suspension. The solvent was removed in vacuo to yield 3.02 g (74%) of compound **6** as a brown solid. Mp: 187 °C decomp (DSC). $[\alpha]_D^{20} = -154°$ (*c* 0.2, dichloromethane). ^{1}H NMR (400.1 MHz, THF-d_8, 300 K): δ 7.24 (m, 2 H, m-Ph), 7.04 (m, 3 H, o,p-Ph), 6.44 and 6.43 (m, each 1 H, 2-/5-H), 5.88 and 5.85 (m, each 1 H, 3-/4-H), 5.20 (m, 1 H, Pro-CH), 4.99 and 4.84 (AX, ^2J = 13.2 Hz, 1 H each, CH_2Ph), 3.53 (m, 2 H, Pro-CH_2N), 2.21, 2.02, 1.90 and 1.72 (m, each 1 H, Pro-CH_2). ^{13}C NMR (100.6 MHz, THF-d_8, 300 K): δ 181.4 (C6), 152.7 (Z-CO), 135.1 (ipso-C of Ph), 125.7 (p-Ph), 125.2 (m-Ph), 124.5 (o-Ph), 112.9 and 110.7 (C2/C5), 113.6 and 112.1 (C3/C4), 63.6 (*C*H_2Ph), 58.9 (Pro-CH), 45.4 (Pro-CH_2N), 31.6 and 21.6 (Pro-CH_2), C1 not detected. Anal. Calcd for $C_{18}H_{18}NO_3Li{\cdot}C_4H_8O$ (375.4): C, 70.39; H, 6.98; N, 3.73. Found: C, 70.34; H, 7.08; N, 3.82.

Preparation of 7. A mixture of **4** (3.00 g, 7.59 mmol) and $FeCl_2$ (0.48 g, 3.79 mmol) in 100 mL of THF was stirred overnight at room temperature. Solvent was removed in vacuo and the residue flash chromatographed at silica gel with pentane/ether (varying ratio from 2:1 to 1:2) containing 1% of *N*,*N*-dimethylethylamine to give 1.88 g (72%) of **7**. Mp: 252 °C (decomp), $[\alpha]_D^{20} = -55°$ (*c* 0.2, dichloromethane). ^{1}H NMR (400.1 MHz, benzene-d_6, 300 K): δ 7.26 (m, 8 H, o-Ph), 7.14 (m, 8 H, m-Ph), 7.07 (m, 4 H, p-Ph), 4.55 and 4.35 (m, each 2 H, 2-/5-H), 3.91 and 3.87 (m, each 2 H, 3-/4-H), 3.95 (q, ^3J = 6.8 Hz, 2 H, −C*H*Me), 3.78 and 3.36 (AX, ^2J = 13.4 Hz, each 4 H, CH_2Ph), 1.35 (d, ^3J = 6.8 Hz, 6 H, CH_3). ^{13}C NMR (100.6 MHz, benzene-d_6, 300 K): δ 202.5 (C=O), 140.1 (ipso-C of Ph), 129.6 (o-Ph), 128.5 (m-Ph), 127.3 (p-Ph), 80.3 (C1), 73.4 and 72.9 (C3/C4), 72.2 and 70.7 (C2/C5), 58.8 (*C*HMe), 54.7 (*C*H_2-Ph), 8.9 (CH_3). Anal. Calcd for $C_{44}H_{44}N_2O_2Fe$ (688.7): C, 76.74; H, 6.44; N, 4.07. Found: C, 76.61; H, 6.75; N, 4.08.

Preparation of 8. A mixture of **4** (395 mg, 1.00 mmol) and 479 mg (0.50 mmol) of $(PPh_3)_3RuCl_2$ in 20 mL of tetrahydrofuran was stirred for 6 h at 60 °C. Solvent was removed in vacuo. The brown residue was taken up in 20 mL of dichloromethane, and the precipitated lithium chloride was removed by filtration. The filtrate was concentrated to dryness and suspended in pentane to remove triphenylphosphine. Solvent was removed from the filtrate and the residue flash chromatographed at silica gel with pentane/ether (4:1) containing 1% of *N*,*N*-dimethylethylamine to yield 177 mg (48%) of **8** as a yellow-brown viscous oil. $[\alpha]_D^{20} = -16°$ (*c* 0.3, dichloromethane). ^{1}H NMR (400.1 MHz, benzene-d_6, 300 K): δ 7.27 (m, 8 H, o-Ph), 7.14 (m, 8 H, m-Ph), 7.06 (m, 4 H, p-Ph), 4.95 and 4.71 (m, each 2 H, 2-/5-H), 4.23 and 4.21 (m, each 2 H, 3-/4-H), 3.82 (q, ^3J = 6.8 Hz, 2 H, −C*H*Me), 3.79 and 3.37 (AX, ^2J = 13.4 Hz, each 4 H, CH_2Ph), 1.33 (d, ^3J = 6.8 Hz, 6 H, CH_3). ^{13}C NMR (100.6 MHz, benzene-d_6, 300 K): δ 200.3 (C=O), 140.1 (ipso-C of Ph), 129.6 (o-Ph), 128.5 (m-Ph), 127.3 (p-Ph), 85.4 (C1), 74.7 and 74.3 (C3/C4), 74.0 and 72.6 (C2/C5), 58.4 (*C*HMe), 54.8 (*C*H_2Ph), 9.1 (CH_3). Anal. Calcd for $C_{44}H_{44}N_2O_2Ru$ (733.9): C, 72.01; H, 6.04; N, 3.82. Found: C, 72.25; H, 6.65; N, 3.37.

Acknowledgment. Financial support from the Fonds der Chemischen Industrie and the Deutsche Forschungsgemeinschaft is gratefully acknowledged.

Supporting Information Available: Description of the preparation and detailed characterization of the compounds **4** and **6** and related reagents and their reaction products with $FeCl_2$ and $(PPh_3)_3RuCl_2$. Details of the X-ray crystal structure analysis of **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM000778T

(9) Velluz, L. Amiard, G.; Heymès, R. *Bull Soc. Chim., Fr.* **1954**, 1012−1015. Velluz, L.; Amiard, G.; Heymès, R. *Bull Soc. Chim., Fr.* **1955**, 201−204.