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of Reliable Methods
for the Preparation
of Organic Compounds

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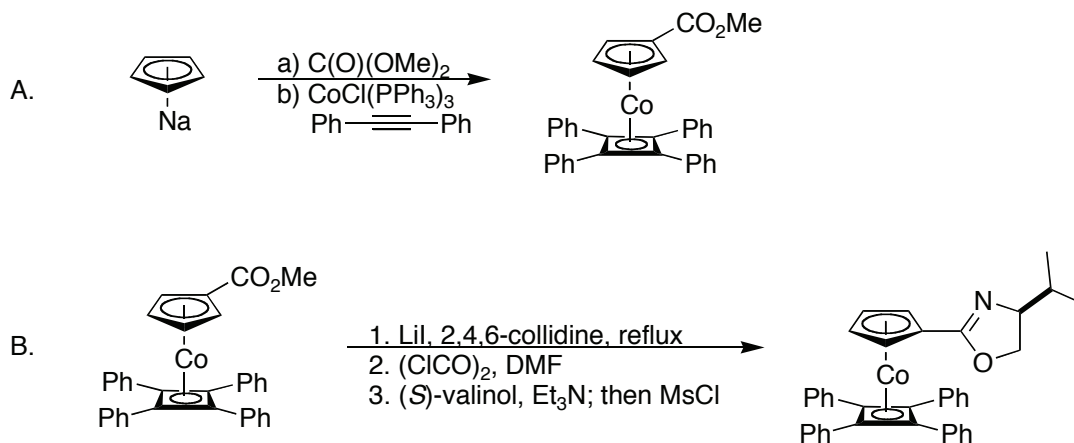
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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**PREPARATION OF (η^5 -(*S*)-2-(4-METHYLETHYL)-
OXAZOLINYLCYCLOPENTADIENYL)-(η^4 -
TETRAPHENYLCYCLO-BUTADIENE)COBALT
(Cobalt, [1,1',1'',1'''-(η^4 -1,3-cyclobutadiene-1,2,3,4-
tetrayl)tetrakis[benzene]][(1,2,3,4,5- η)-1-[(4*S*)-4,5-dihydro-4-(1-
methylethyl)-2-oxazolyl]-2,4-cyclopentadien-1-yl])**



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Checked by Joshua Bolger and Marvin J. Miller.

1. Procedure

A. Preparation of (η^5 -carbomethoxycyclopentadienyl)-(η^4 -tetraphenyl-cyclobutadiene)cobalt. A flame-dried, 500-mL, three-necked, round-bottomed flask is fitted with a stirring bar, reflux condenser, rubber septa, and an argon inlet. The flask is flushed with dry argon and charged with sodium cyclopentadienide (Note 1) (20 mL, 2.0 M in THF, 40 mmol) and 20 mL of anhydrous tetrahydrofuran (Note 2) via syringe. Dimethyl carbonate (Note 1) (10.2 mL, 120 mmol) is added via syringe and the resulting solution is warmed to reflux for 4 h before cooling to room temperature (Note 3).

Once cooled, 160 mL of toluene (Note 2) is added via syringe, followed by chlorotris(triphenylphosphine)cobalt(I) (Note 4) (30.8 g, 34.8 mmol) and diphenylacetylene (Note 5) (14.2 g, 80 mmol) by temporarily removing a rubber septum. The resulting mixture is heated at reflux for 5 h before cooling to room temperature, transferring to a single-neck flask, and concentrating under reduced pressure. The residue is suspended in hexanes

(150 mL) and filtered through a Büchner funnel. The solids are washed with hexanes (~3.5 L) until the filtrate is colorless. The resultant dark mustard-colored filter cake is dissolved from the filter into a new collection flask with methylene chloride. Washing is continued until the filtrate is colorless. A black insoluble solid is left after washing and is discarded. The organic solution is concentrated *in vacuo* to provide 12.7 g (23.6 mmol, 67%) of (η^5 -carbomethoxycyclopentadienyl)-(η^4 -tetraphenylcyclobutadiene)cobalt as a mustard-colored solid (Notes 6, 7).

B. Preparation of (η^5 -(S)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4 -tetraphenylcyclobutadiene)cobalt. A flame-dried, 250-mL, round-bottomed flask is fitted with an air condenser, stirring bar and an argon inlet. The flask is flushed with dry argon and then charged with (η^5 -carbomethoxycyclopentadienyl)-(η^4 -tetraphenylcyclobutadiene)cobalt (10 g, 18.6 mmol), lithium iodide (Note 8) (4.95 g, 37.2 mmol), and 100 mL of 2,4,6-collidine (Note 1) by temporarily removing the condenser. The resulting solution is warmed to reflux. After 16 h, the solution is cooled to room temperature (Note 9) and diluted with 50 mL of methylene chloride. This solution is washed with 150 mL of 2 N aqueous hydrochloric acid, and the aqueous layer is extracted with 150 mL of methylene chloride. The combined organic phases are then washed with 2 N aqueous hydrochloric acid (4 x 150 mL), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to provide (η^5 -carboxycyclopentadienyl)-(η^4 -tetraphenylcyclobutadiene)cobalt as an orange solid (Note 10), which is used directly in the next transformation.

A flame-dried, 250-mL, round-bottomed flask is fitted with a stirring bar and an argon inlet. The flask is flushed with argon and then charged with crude (η^5 -carboxycyclopentadienyl)-(η^4 -tetraphenylcyclobutadiene)cobalt and 124 mL of methylene chloride (Note 2). Oxalyl chloride (Note 1) (3.25 mL, 37.2 mmol) and dimethylformamide (Note 11) (3 drops) are added sequentially. Upon addition of the latter, gas evolution is observed. The resulting solution is maintained at room temperature. After 30 min, the solution is concentrated using a rotary evaporator. Volatile byproducts and excess starting materials are removed by dissolving the residue in 100 mL of methylene chloride and concentrating this solution using a rotary evaporator. The evaporation procedure is repeating three times to provide the corresponding acid chloride as a red-brown residue, which is used directly in the next transformation.

A flame-dried, 500-mL, round-bottomed flask is fitted with a stirring bar and a septum containing argon inlet and outlet needles. The flask is flushed with argon and then charged with (*S*)-valinol·HCl salt (Note 12) (3.6 g, 26 mmol) by temporarily removing the septum, triethylamine (Note 11) (15.5 mL, 112 mmol) and 86 mL of methylene chloride (Note 2) via syringe. A solution of crude acid chloride and 100 mL of methylene chloride (Note 2) is added to the flask via cannula. The resulting solution is maintained at room temperature, and, after 2 h, the solution is cooled to 0 °C using an ice/water bath. Methanesulfonyl chloride (Note 1) (3.6 mL, 47 mmol) is then added in one portion via syringe, and the resulting solution is allowed to warm to room temperature. After 16 h, the solution is transferred to a separatory funnel and washed with 150 mL of saturated aqueous sodium bicarbonate and 150 mL of brine. The organic layer is then dried over anhydrous sodium sulfate, filtered, and concentrated using a rotary evaporator. The residue is dissolved in a minimum volume of methylene chloride (~50 mL) and purified through a column of silica gel using 9:1 hexanes-ethyl acetate as eluent (Note 13). Evaporation of solvent gives 8.2 g (13.9 mmol, 75% yield) of (η^5 -(*S*)-2-(4-methylethyl)oxazolinylcyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt as a yellow solid (Note 14).

2. Notes

1. Sodium cyclopentadienide was purchased from Aldrich Chemical Company or Strem Chemical. This reagent should be light red/orange in color. Commercial reagent that is black in color and/or contains some solid residue should not be used. Dimethyl carbonate, oxalyl chloride, methanesulfonyl chloride, and 2,4,6-collidine were purchased from Acros Organics or Aldrich Chemical Company. These chemicals were used as received.

2. Tetrahydrofuran, toluene and methylene chloride were purified by passage through activated alumina using a GlassContour solvent purification system.² The checkers used anhydrous Acroseal solvents.

3. Sodium carbomethoxycyclopentadienide can be isolated,³ but its isolation and purification were unnecessary for this procedure.

4. Chlorotris(triphenylphosphine)cobalt(I) was prepared according to a detailed literature procedure.⁴ This reagent could be purchased from Aldrich Chemical Company. However, it is quite expensive; the use of the commercial material typically resulted in lower yields of product.

5. Diphenylacetylene was purchased from Acros Organics and was recrystallized from ethanol prior to use.

6. Somewhat higher yield (13.8 g, 25.6 mmol, 74%) was observed when the solution of sodium carbomethoxycyclopentadienide and THF was transferred by cannula to a 500-mL round-bottomed flask charged with dichlorotris(triphenylphosphine)cobalt(I), diphenylacetylene and toluene. However, this procedure was less convenient.

7. The product, (η^5 -carbomethoxycyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt, showed the following characterization data; ^1H NMR (500 MHz, CDCl_3) δ : 3.23 (s, 3 H), 4.79 (t, $J = 2.0$ Hz, 2 H), 5.21 (t, $J = 2.0$ Hz, 2 H), 7.22–7.30 (m, 12 H), 7.43–7.45 (m, 8 H); ^{13}C NMR (125 MHz, CDCl_3) δ : 51.4, 76.5, 84.7, 86.6, 86.8, 126.9, 128.2, 129.0, 135.3, 166.6; Infrared spectrum (thin film) cm^{-1} : 3058, 2953, 1713, 1596, 1498, 1467, 1281, 1140; HRMS (FAB+) m/z 538.1320 [538.1343 calcd for $\text{C}_{35}\text{H}_{27}\text{O}_2\text{Co}$ (M^+)]; Anal. Calcd. for $\text{C}_{35}\text{H}_{27}\text{O}_2\text{Co}$: C, 78.06; H, 5.05. Found: C, 78.30; H, 5.43.

8. Lithium iodide was purchased from Acros Organics. In some instances, the use of old bottles of this reagent resulted in incomplete conversion.

9. The disappearance of starting material could be monitored by TLC analysis. Using 20% ethyl acetate: hexanes as eluent, (η^5 -carbomethoxycyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt had an R_f of 0.8.

10. The crude product, (η^5 -carboxycyclopentadienyl)(η^4 -tetraphenylcyclobutadiene)cobalt, showed the following ^1H NMR spectrum; (500 MHz, CDCl_3) δ : 4.84 (2d, $J = 2.0$ Hz, 2 H), 5.23 (2d, $J = 2.0$ Hz, 2 H), 7.20–7.24 (m, 12 H), 7.42–7.44 (m, 8 H).

11. Dimethylformamide and triethylamine were purified by passage through GlassContour solvent purification columns.² The checkers used anhydrous dimethylformamide purchased from Acros Organics. Triethylamine was purchased from Aldrich Chemical Company and used as received.

12. (*S*)-Valinol was prepared by reduction of (*S*)-valine.⁵ The checkers used (*S*)-valinol purchased from Aldrich Chemical Company, Inc. The salt was formed by treatment of the freebase with 2 N HCl in diethylether.

13. The submitters reported dissolving the crude residue in 9:1 hexanes:EtOAc prior to loading on the column, but the checkers isolated 5.6

g (9.5 mmol, 51% yield) of pure product by filtration of the resulting slurry. The residue remaining after concentration of the filtrate was dissolved in a minimum of methylene chloride and purified as described to give an additional 2.6 g (4.4 mmol, 24% yield) of the pure product. Subsequent reactions were purified exclusively by column chromatography.

14. The product, $(\eta^5\text{-(S)-2-(4-methylethyl)oxazolinylcyclopentadienyl})\text{-(}\eta^4\text{-tetraphenylcyclobutadiene)cobalt}$, shows the following characterization data; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ : 0.76 (d, $J = 7.0$ Hz, 3 H), 0.98 (d, $J = 6.5$ Hz, 3 H), 1.37–1.44 (m, 1 H), 3.41–3.55 (m, 3 H), 4.71 (2d, $J = 2.5$ Hz, 2 H), 4.8 (2d, $J = 2.5$ Hz, 2 H), 5.09 (s, 1 H), 5.25 (brs, 1 H) 7.20–7.29 (m, 12 H), 7.45–7.47 (m, 8 H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ : 18.4, 19.6, 33.0, 69.5, 72.7, 76.0, 82.0, 84.4, 85.0, 86.4, 126.4, 128.0, 129.0, 135.4, 160.5; Infrared spectrum (thin film) cm^{-1} : 3058, 2958, 1652, 1597, 1499, 1373, 1113, 1024; HRMS (FAB+) m/z 592.2055 [592.2051 calcd for $\text{C}_{39}\text{H}_{35}\text{CoNO (M+H)}$]. Anal. Calcd. for $\text{C}_{39}\text{H}_{34}\text{ONCo}$: C, 79.17; H, 5.79; N, 2.37. Found: C, 79.12; H, 5.83; N, 2.33.

Safety and Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with “Prudent Practices in the Laboratory”; National Academy Press; Washington, DC, 1995.

3. Discussion

This synthesis of $(\eta^5\text{-(S)-2-(4-methylethyl)oxazolinylcyclopentadienyl})\text{-(}\eta^4\text{-tetraphenylcyclobutadiene)cobalt}$ is a modification of a procedure originally reported by Richards and Stevens.⁶ The procedure has been streamlined and modified to enable large-scale preparation of this oxazoline. Nucleophilic conditions, rather than hydrolytic, are used to cleave the ester to the acid in Step B, thereby eliminating the use of DMSO, which is difficult to remove. Removal of DMSO is an essential feature of the original procedure as oxalyl chloride is employed in the following step.⁶ In the present procedure, the oxazoline is formed directly from the crude valinol amide by reaction with methanesulfonyl chloride and triethylamine in methylene chloride. These conditions eliminate the need for toxic carbon tetrachloride; previously the isolated valinol amide was cyclized using triphenylphosphine, carbon tetrachloride and triethylamine.⁶ In this

optimized procedure, conversion of the ester to the oxazoline is accomplished in one pot.

(η^5 -(*S*)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4 -tetraphenylcyclobutadiene)cobalt is an intermediate in the synthesis of the planar, chiral palladium(II) catalysts, [COP-Cl]₂,⁷ [COP-OAc]₂,⁷ and COP-hfacac,⁷ which have been used in the catalytic asymmetric synthesis of chiral allylic amides^{8,9} and allylic esters.¹⁰ This procedure illustrates a general synthesis of enantiopure (η^5 -(*S*)-2-oxazolinylcyclopentadienyl)-(η^4 -tetraphenylcyclobutadiene)cobalt complexes. Analogous oxazoline complexes prepared from (*S*)-serine have been used as ligands for catalytic asymmetric addition of organozinc reagents to aldehydes and palladium-catalyzed allylic alkylations.¹¹ As enantioenriched monodentate oxazolines have found use as chiral ligands,¹² and η^5 -(cyclopentadienyl)-(η^4 -tetraphenylcyclobutadiene)cobalt complexes have been used to prepare a variety of novel materials,¹³ the oxazoline product of this procedure could find use in its own right.

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Appendix

Chemical Abstracts Nomenclature; (Registry Number)

(η^5 -Carbomethoxycyclopentadienyl)-(η^4 -tetraphenylcyclobutadiene)cobalt;
(182627-81-2)

Sodium cyclopentadienide: Sodium, 2,4-cyclopentadien-1-yl-; (4984-82-1)

Chlorotris(triphenylphosphine)cobalt(I); (26305-75-9)

Diphenylacetylene: Benzene, 1,1'-(1,2-ethynediyl)bis-; (501-65-5)

Lithium iodide; (10377-51-2)

2,4,6-Collidine: Pyridine, 2,4,6-trimethyl-; (108-75-8)

Oxalyl Chloride: Ethanedioyl dichloride; (79-37-8)

N,N-Dimethylformamide; (68-12-2)

(*S*)-Valinol: 1-Butanol, 2-amino-3-methyl-, (2*S*)-; (2026-48-4)

Triethylamine: Ethanamine, *N,N*-diethyl-; (121-44-8)

Methanesulfonyl chloride; (124-63-0)



Larry Overman was born in Chicago, Illinois, in 1943 and raised in Hammond, Indiana. He obtained a B.A. degree from Earlham College in 1965 and completed his doctoral dissertation in 1969 with Professor Howard W. Whitlock, Jr. at the University of Wisconsin. After a NIH postdoctoral fellowship with Professor Ronald Breslow at Columbia University, he joined the faculty at the University of California, Irvine in 1971 where he is now Distinguished Professor of Chemistry. Professor Overman was Chair of the UC Irvine Department of Chemistry from 1990–1993.



Carolyn Anderson received her B.Sc. degree in Chemistry from the University of Michigan in 1998 and her Ph.D. in Chemistry from the University of California at Irvine (with Larry Overman) in 2003. She was a Dreyfus Postdoctoral Fellow at Pomona College (Claremont, California) under the mentorship of Daniel O’Leary (2004–2006). In 2006, she joined the faculty of Calvin College (Grand Rapids, Michigan) as an Assistant Professor of Chemistry. Her current research interests include using organometallic methods to synthesize libraries of strained carbocycles.



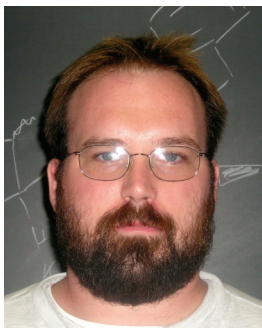
Chris Richards was born in Woking, England, and obtained a B.Sc degree in Chemistry from the University of Bath in 1989. This was followed by a Ph.D. in 1990 working with Professor Sue Gibson at the University of Warwick. After spending 1 year as an Alexander von Humboldt Research Fellow with Professor Helmchen at the University of Heidelberg, he took up a Lectureship at Cardiff University in Wales. In 2001 he moved to his current position of Reader at Queen Mary, University of London. His research interests encompass organometallic chemistry, organic synthesis, stereochemistry and catalysis.



Mary P. Watson received her B.A. from Harvard University in 2000, where she studied organic chemistry under the direction of Prof. David Evans. She then moved to University of California, Irvine, to work with Prof. Larry Overman. Her graduate research focused on the palladium(II)-catalyzed asymmetric allylic imidate rearrangement, including mechanistic studies performed in collaboration with Prof. Robert Bergman at the University of California, Berkeley. During her graduate work, she received the Allergan graduate student fellowship. She received her Ph.D. in 2006 and is currently a postdoctoral researcher at Harvard University with Prof. Eric Jacobsen.



Nicole S. White received her B.S. from the University of California, San Diego, in 2002. She then accepted a position in the medicinal chemistry department of Neurocrine Biosciences, where she worked on development of an MC4 antagonist aimed towards the treatment of cachexia. In 2004 she moved to the University of California, Irvine, to work with Prof. Larry Overman. Currently, her graduate research focuses on the use of palladium(II) catalysts to construct carbon–heteroatom bonds asymmetrically.



Joshua Bolger received his B.S. in chemistry from the Rochester Institute of Technology in 2000. While at RIT he worked as an intern at AstraZeneca, synthesizing CNS active molecules, and Eastman-Kodak Company, synthesizing photosensitizing dyes for silver-halide film. After receiving his B.S. he joined OSI Pharmaceuticals, Inc. where he worked on a number of projects in the fields of Diabetes/Obesity and Oncology. In 2003 Joshua began his graduate education joining the laboratory of Dr. Marvin J. Miller at the University of Notre Dame. He is currently in his fourth year of research focusing on the synthesis of bioactive molecules using Acylnitroso Diels-Alder reactions.

