to bertyadionol;[27] complete destruction of the molecule, to say nothing of epimerization, occurred. Second, all attempts to remove the dithioketal exploiting most, if not all, of the known procedures (ca. 23),[28] proved uniformly unsuccessful. Fortunately, a deprotection–dithioketal hydrolysis protocol was eventually developed. The sequence involved removal of the benzoate [2 N NaOH, MeOH, Pyr (1:2:2), 63%], oxidation of the dithioketal functionality (*m*-CPBA, CH_2Cl_2, 0 °C) to the monosulfoxide, and then a "Pummerer-like" hydrolysis [Ac_2O, Et_3N, aqueous THF (3:4:10), 40 °C]. The result was a thermodynamic mixture (45:55) of bertyadionol (**1**) and its C(2) epimer,[20a] which was readily separable by HPLC (15% hexane–ethyl acetate, Ultrasphere-SI). The yield for the oxidative-hydrolysis maneuver was 28–37%. That in fact synthetic (−)-bertyadionol [mp 157–158.5 °C; lit.[8] 159–160 °C; $[\alpha]^{24}_D$ −318° (*c* 0.04, benzene, 89% ee), authentic **1** $[\alpha]^{24}_D$ −356° (*c* 0.10, benzene)],[27] was in hand derived from careful comparison (^{1}H NMR, TLC, HPLC, mp, mmp, and GC/MS) with an authentic sample of natural (−)-bertyadionol kindly provided by Professor Jefferies.[27]

In summary, the first total synthesis of a lathyrane diterpene, (−)-bertyadionol, has been achieved. The synthesis delivered the target in homochiral form. Of particular interest is the rapid assembly of the carbon skeleton, the viability of the intramolecular ketophosphonate construction of the 11-membered ring, and the oxidative protocol for the hydrolysis of dithioketals. Studies to exploit this strategy for the synthesis of other members in this class will be reported in due course.

Acknowledgment. Support for this investigation was provided by the National Institutes of Health through Grant GM-29028 and by Merck Sharp & Dohme Research Laboratories.

Supplementary Material Available: Physical data for selected intermediates (2 pages). Ordering information is given on any current masthead page.

(27) We thank Professor P. R. Jefferies (University of Western Australia) for the generous samples of (−)-bertyadionol and (−)-bertyadionol acetate.
(28) For an excellent review, see: Grobel, B.-T.; Seebach, D. *Synthesis* **1977**, 357.

Total Synthesis of (+)-Rosaramicin Aglycone and Its Diacetate†

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Rosaramicin, a macrocyclic lactone isolated from the fermentation broth of *Micromonospora rosaria* NRRL-3718, is a potent broad spectrum antibiotic of considerable clinical interest.[3] This natural product is characteristic of its class and provides an interesting test of an anti-selective aldol method developed in these laboratories.[4]

Our construction of **1** commences with the key tactical component, namely, combination of the vinylogous urethane **3**, via its lithium enolate, with the chiral aldehyde **4** to obtain the lactone **5**. This substance leads to the acid **6** which on esterification with the alcohol aldehyde **7** followed by cyclo-olefination, alcohol deprotection, and epoxidation completes the synthesis of **1**, permitting, for the first time, the characterization of this aglycone.[5]

Deprotonation of **3**[6] (LDA, THF, 0.75 M, −78 °C, 90 min) generates the enolate **8**[7] which on treatment with the aldehyde **4**[6] (THF, 1.4 M, −78 °C, 30 min; 0 °C, 10 h) affords an 8:1 mixture of lactone products epimeric at C_4. The major isomer **5**, $[\alpha]_D$ +54.3° (*c* 1.0, CH_2Cl_2), was separated from its epimer by flash chromatography (70%). **5** was reduced and methylated (Li, NH_3; CH_3I) and the resulting saturated β-amino lactone converted into its *N*-oxide and eliminated (*m*-CPBA/Et_3N) to give (60% from **5**) the unsaturated lactone **9**, $[\alpha]_D$ +44.3° (*c* 1.5, CH_2Cl_2).

Conversion of **9** into the saturated lactone **10** was accomplished by diisobutylaluminum hydride reduction of the lactone to give a mixture of lactol anomers. Without purification, this material was persilylated with trimethylsilyl chloride under basic conditions (C_5H_5N, CH_2Cl_2) to give (88% from **9**) compound **11**, $[\alpha]_D$ +37.4° (*c* 1.0, CH_2Cl_2). The trisubstituted olefinic residue of **11** was then reduced, although not without difficulty, by using rhodium 5% on alumina (THF, 22 °C, H_2 >2000 psi, 120 h). Treatment of the crude reduction product with methanolic K_2CO_3 (22 °C, 3 h) to remove the trimethylsilyl groups followed, again without purification, by Collins oxidation (22 °C, 30 min) resulted (90% yield from **11**) in the aldehyde lactone **10**, $[\alpha]_D$ +31.7° (*c* 1.5, CH_2Cl_2), as a single substance carrying the C_2 methyl group in the required β-configuration.

We next converted the aldehyde portion of **10** into its dimethyl acetal analogue using trimethyl orthoformate and pyridinium *p*-toluenesulfonate in toluene. This intermediate was then treated with *p*-toluenesulfonic acid in methanol (0 °C, 1 h), which not only ring-opened the lactone into a methyl ester but also caused the conversion of the acetal residue into a five-membered-ring lactolide as well as removed the *tert*-butyldimethylsilyl group present on the side chain of **10**. The product formed by this process, **12**, $[\alpha]_D$ +36.3° (*c* 1.5, CH_2Cl_2), was obtained (66% yield from **10**) as a 6:1 mixture of anomers.[8] Interestingly, the direct conversion of **10** into **12**, while possible, occurred in significantly lower yield. The methyl ester residue of **12** reacted smoothly (90% yield) with dimethyl (lithiomethyl)phosphonate to give **13**, $[\alpha]_D$ +62.2° (*c* 1.0, CH_2Cl_2).

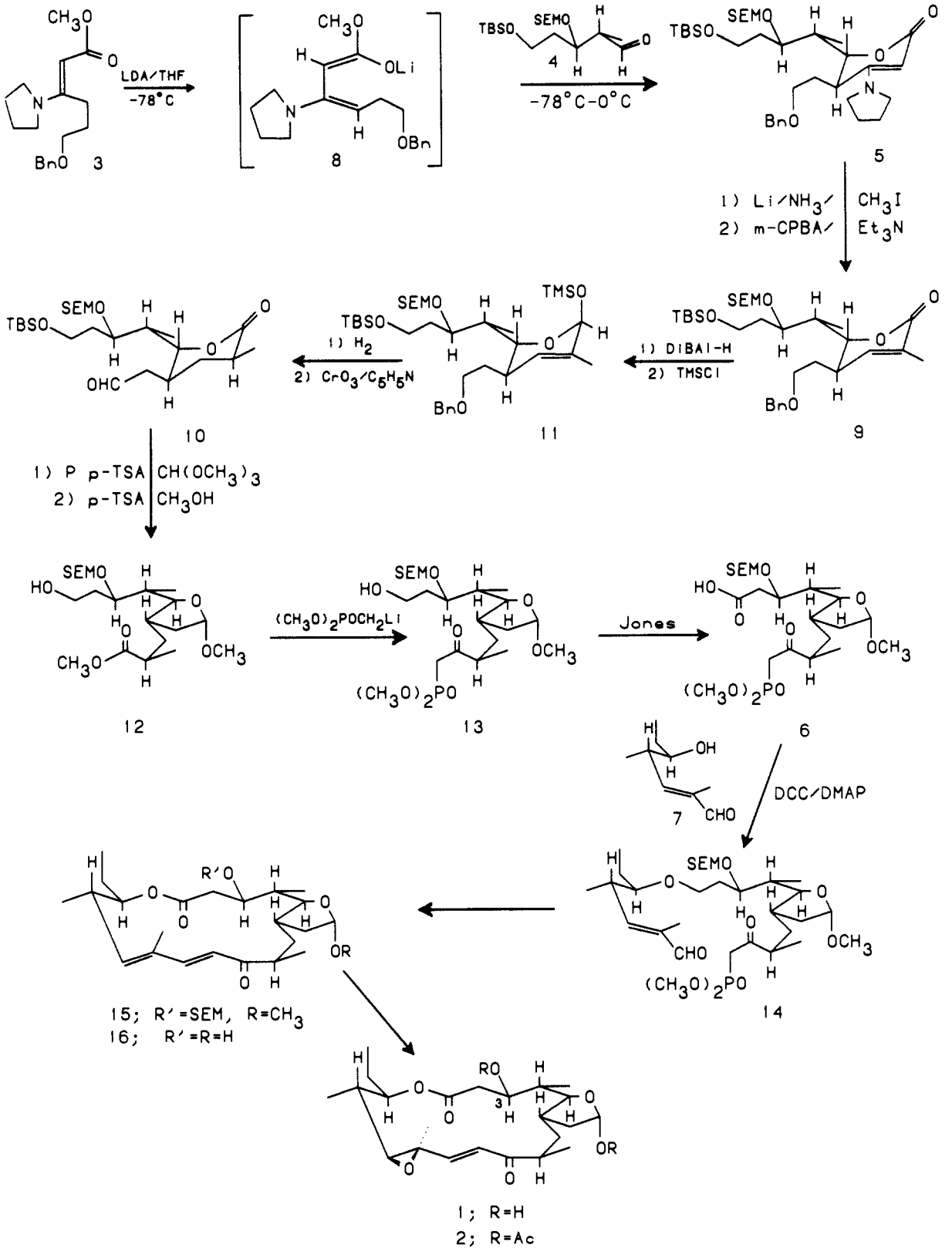
Jones oxidation (−20 °C) of **13** gave the acid **6**[9] which was immediately esterified with the alcohol aldehyde **7** through the agency of DCC and 4-(dimethylamino)pyridine in CH_2Cl_2 to give (66% yield from **13**) the ester **14**, $[\alpha]_D$ +63.3° (*c* 1.0, CH_2Cl_2), after flash chromatography.[10] Cyclo-olefination of **14** into **15**, $[\alpha]_D$ −11.3° (*c* 1.0, CH_2Cl_2), occurred in gratifying yield (85% after flash chromatography), using K_2CO_3 and 18-crown-6 in toluene (70 °C, 5 h).[11]

After considerable experimentation, it was found that **16**, $[\alpha]_D$ +7.8° (*c* 1.42, CH_2Cl_2), as a 3:1 mixture of anomers, could be obtained from **15** by employing 90% trifluoroacetic acid (0 °C, 10 min). Epoxidation of **16** using an aqueous pH 8 buffer (*m*-CPBA, CH_2Cl_2, 0 °C, 7 h),[12] afforded **1**, $[\alpha]_D$ +20.0° (*c* 1.10, CH_2Cl_2), as a 3:1 mixture of anomers, mp 212–213 °C, from **15**

† Dedicated to Professor Marshall D. Gates on the occasion of his 70th birthday.
(1) Hooker Corp. Fellow, Sherman Clarke Fellow, ACS Graduate Fellow in Organic Chemistry.
(2) Sherman Clarke Fellow.
(3) (a) Wagman, G. H.; Waitz, J. A.; Muarwski, A.; Oden, E. M.; Testa, R. T.; Weinstein, M. J J. *Antibiot.* **1972**, *21*, 641. (b) Stamm, W. E.; Holmes, K. K. *Abstract from Sexually Transmitted Diseases*, 2nd Meeting, Helsinki, Finland, Aug 9–10, 1979. (c) Maragoni, F.; Dainelli, B.; Magni, A.; Scazzocchio, F.; Repetto, A.; Filadoro, F. *Chemioterapia* **1983**, *2*, 56.
(4) For other applications of this anti-selective aldol method within the context of a total synthesis, see: (a) Schlessinger, R. H.; Bebernitz, G. R.; Lin, P.; Poss, A. J. *J. Am. Chem. Soc.* **1985**, *107*, 1777. (b) Schlessinger, R. H.; Poss, M. A. *J. Am. Chem. Soc.* **1982**, *104*, 357.
(5) A synthesis of the 3-deoxy aglycone of rosaramicin has been reported by: Still, W. C.; Novack, V. J. *J. Am. Chem. Soc.* **1984**, *106*, 1148. Somewhat to our surprise, however, rosaramicin aglycone, **1**, has never been described.
(6) Details for the preparation of all new materials mentioned in the text together with spectral data on them are available as supplemental material.
(7) Data supporting the structure of enolate **8** will be submitted for publication, manuscript in preparation.
(8) This 6:1 anomeric mixture is maintained throughout the reaction sequence leading to **1** until the penultimate step.
(9) For a leading reference, see: Ziegler, F. E.; Berger, G. D. *Synth. Commun.* **1979**, *9*, 539.
(10) The workup procedure for this reaction followed that outlined in the literature by: Muller, R. H; DiPardo, R. M. *J. Org. Chem.* **1977**, *42*, 3210.
(11) For leading references, see: (a) Aristoff, P. A. *J. Org. Chem.* **1981**, *46*, 1954. (b) Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R. *J. Am. Chem. Soc.* **1982**, *104*, 2030.
(12) Imuta, M.; Ziffer, H. *J. Org. Chem.* **1979**, *44*, 1351.

0002-7863/86/1508-3112$01.50/0

Scheme I



in 67% overall yield (Scheme I).

Since **1** was an unknown substance that could not be obtained by degradation of the natural product, we converted it (92% yield) into its corresponding diacetate **2**[13] with acetic anhydride in pyridine containing DMAP at 0 °C. Synthetic **2**, $[\alpha]_D$ +18.4° (*c* 1.63, CH_2Cl_2, mp 174–175 °C), was isolated as an 8:1 mixture of anomers. In addition, diacetate **2** (mp 174–175 °C) was prepared by degradation of rosaramicin.[14] In this instance, **2** was isolated as a 3:1 mixture of anomers and showed an optical rotation of $[\alpha]_D$ +11.4° (*c* 1.62, CH_2Cl_2).[15] Since synthetic and natural

(13) Ganguly, A. K.; Liu, Y.-T.; Sarre, O.; Jaret, R. S. *Tetrahedron Lett.* **1972**, *13*, 1270.

(14) Special thanks to Professor W. Clark Still (Columbia University) and Dr. Ashit Ganguly (Schering Corp.) for an experimental protocols describing the degradation of rosaramicin into the diacetate **2**. Full details on the physical data for synthetic **2** and for **2** obtiained from the natural product are available in the supplemental material.

2 were different anomeric mixtures, they were hydrolyzed into their corresponding C_3 monoacetates.[14] Both synthetic and naturally derived substances proved to be the same 3.7:1 anomeric mixture and, finally, exhibited the same properties: $[\alpha]_D$ -9.8° (c 1.43, CH_2Cl_2) natural series, $[\alpha]_D$ -9.7° (c 0.51, CH_2Cl_2) synthetic series.

Acknowledgment. We thank Dr. G. R. Bebernitz for the preparation of some intermediates leading to compound **7**. We thank Dr. Ashit Ganguly (Schering Corp.) for a generous sample of rosaramicin. Financial support from the NIH and the Merck Corp. are gratefully acknowledged.

Supplementary Material Available: Experimental procedures including NMR, IR, and mass spectral data (71 pages). Ordering information is given on any current masthead page.

(15) Both synthetic and naturally derived **2** were crystallized from ethyl acetate/hexane. A mixed melting point of these materials was undepressed.

Synthesis of a New Type of Metal Dithiolene Complex via an Induced Reaction of Acetylenes with a Ruthenium Sulfide

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The reactions of unsaturated organic compounds with naked main-group ligands is an active area of coordination chemistry.[1] The present contribution to this field involves the chemically induced reaction of a soluble ruthenium sulfide with acetylenes. This project has resulted in the characterization of the simplest ruthenium sulfido complex and a unique bonding mode for a 1,2-alkene disulfide (dithiolene) ligand.

Our starting material was $Cp^*_2Ru_2S_4$ (**1**, $Cp^* = \eta^5$-C_5Me_4Et), a highly soluble, air-stable, intensely blue compound.[2] Compound **1** was prepared in ca. 15% yield from the reaction of 3.02 g of $Cp^*_2Ru_2(CO)_4$[3] and 0.62 g of S_8 in 125 mL of boiling toluene for 18 h. The crude product was flash chromatographed on silica gel (CH_2Cl_2) and crystallized from cold hexane. An X-ray diffraction study showed that **1** is properly formulated as $Cp^*_2Ru_2(\mu,\eta^2\text{-}S_2)(\mu,\eta^1\text{-}S_2)$ comparable to the recently reported iron analogues.[4] Whereas the Ru-S distances are normal for the μ,η^2-S_2, the Ru-S distances for the parallel (μ,η^1) S_2 are quite short at 2.20 Å and indicate multiple bonding[5] between the ruthenium centers and this disulfur ligand.

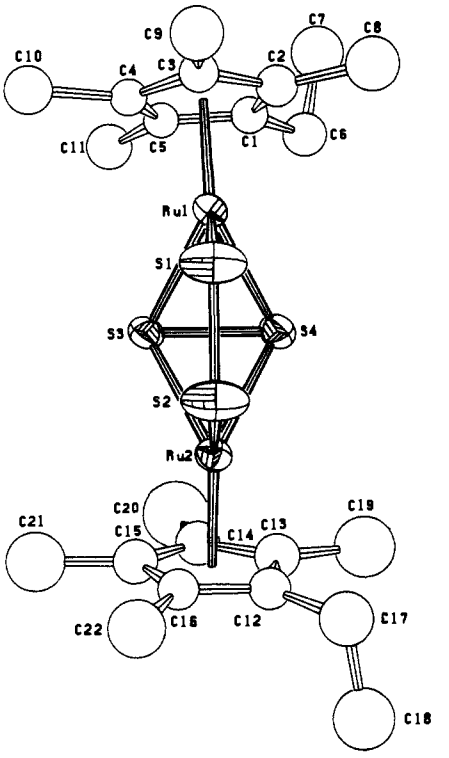

Figure 1. ORTEP of the $(C_5Me_4Et)_2Ru_2S_4$ molecule (**1**). Representative distances (Å) and angles (deg): Ru(1)-S(1), 2.195 (4); Ru(1)-S(3), 2.382 (4); S(1)-S(2), 2.020 (5); S(3)-S(4), 2.050 (4); Ru(1)-S(1)-S(2), 112.9 (2); Ru(1)-S(3)-Ru(2); 104.1 (1); Ru(1)-S(3)-S(4), 64.9 (1). The S···S distances between the two S_2 subunits are 3.39-3.42 Å.

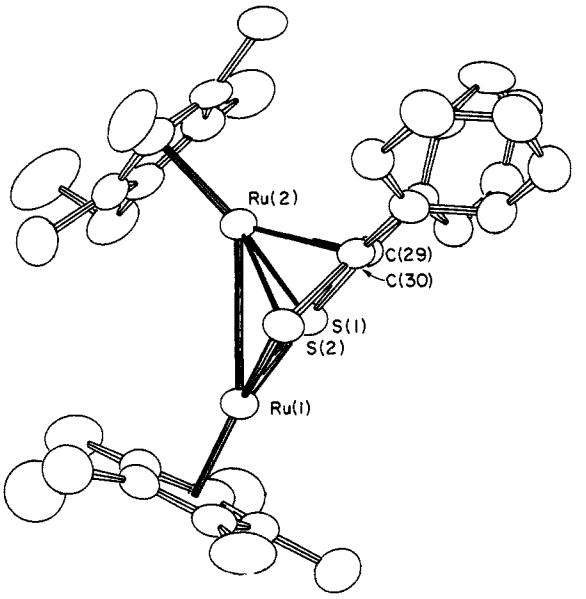

Figure 2. ORTEP of the $(C_5Me_4Et)_2Ru_2S_2C_2Ph_2$ molecule (**3**). Representative distances (Å) and angles (deg): Ru-Ru, 2.980 (1); Ru(1)-S(1), 2.253 (3); Ru(2)-S(1), 2.428 (3); Ru-Si(1)-Ru, 79.00 (8); Ru(1)-S(1)-C(29), 109.5 (3); Ru(2)-S(1)-C(29), 60.7 (3).

A compound tentatively identified as $Cp^*_4Ru_4S_6$ (**2**) was also isolated in ca. 20% yield in the synthesis of **1**.[6] Compound **2** is

(1) (a) Oxide reactions: Groves, J. T.; Watanabe, Y. *J. Am. Chem. Soc.* **1986**, *108*, 507. Collman, J. P.; Kodadek, T.; Raybuck, S. A., Brauman, J. T.; Papazian, L. M. *J. Am. Chem. Soc.* **1985**, *108*, 507. Herrmann, W. A.; Serrano, R.; Küsthardt, U.; Ziegler, M. L.; Guggolz, E., Zahn, T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 515. (b) Sulfide reactions: Adams, R. D.; Wang, S. *Organometallics* **1985**, *4*, 1902. Rajan, O. A.; McKenna, M.; Noordik, J.; Haltiwanger, R. C., Rakowski DuBois, M. *Organometallics* **1984**, *3*, 831. Bolinger, C. M.; Rauchfuss, T. B.; Rheingold, A. L. *J. Am. Chem. Soc.* **1983**, *103*, 6321. (c) Phosphinidine reactions: Lunnis, J.; MacLaughlin, S. A.; Taylor, N. J.; Carty, A. J.; Sappa, E. *Organometallics* **1985**, *4*, 2066. Marinetti, A.; Mathey, F. *Organometallics* **1984**, *3*, 456.

(2) Anal C, H, S. FABMS (*m/z*, ^{102}Ru) 630 (P^+); ^{1}H NMR (δ in ppm, *J* in Hz, $CDCl_3$) 2.23 (q, 4 H, 7.3), 1.92 (s, 12 H), 1.87 (s, 12 H), 1.10 (t, 6 H, 7.4). Compound **1** crystallized from hexane in the space group $P\bar{1}$, with cell dimensions a = 18.386 (4) Å, b = 18.868 (4) Å, c = 8.564 (3) Å, α = 98.64 (2)°, β = 91.12 (2)°, γ = 117.48 (2)°, V = 2592 (1) Å^3, Z = 4, ρ_{exp} = 1.60 g cm^{-3}, for $\pm h,\pm k,+l$ in the range 3.0° < 2θ < 46°. These data were averaged to (R_{av} = 0.018). The structure 7256 independent reflections was solved by direct methods (SHELX), refined with use of 4377 intensities ($I > 2.58\ \sigma(I)$) to R = 0.053 and R_w = 0.067.

(3) Bailey, N. A.; Radford, S. L.; Sanderson, J. A.; Tabatabaian, K.; White, C.; Worthington, J. M. *J. Organomet. Chem.* **1978**, *154*, 343.

(4) Chenaud, H.; Ducourant, A. M.; Giannotti, C. *J. Organomet. Chem.* **1980**, *190*, 201. Weberg, R.; Haltiwanger, R. C.; Rakowski DuBois, M. *Organometallics* **1985**, *4*, 1315. Brunner, H.; Janietz, N.; Meier, W.; Sergeson, G.; Wachter, J.; Zahn, T.; Ziegler, M. L. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1060.

(5) Millar, M. M.; O'Sullivan, T.; de Vries, N.; Koch, S. A. *J. Am. Chem. Soc.* **1985**, *107*, 3714.

(6) Anal. C, H, S. FDMS (*m/z*, ^{102}Ru) 1196 (P^+), 1164 (P^+ - S), 1132 (P^+ - 2S), 1047 (P^+ - Cp*); ^{1}H NMR (see ref 2, C_6D_6) 2.45 (q, 2 H, 7.5), 2.31 (q, 4 H, 7.7), 2.11 (m, 8 H), 2.05 (s, 6 H), 1.78 (s, 6 H), 1.77 (s, 6 H), 1.69 (s, 6 H), 1.64 (s, 6 H), 1.63 (s, 6 H), 1.60 (s, 6 H), 1.24 (t, 3 H, 7.60), 0.98 (t, 6 H, 7.4), 0.89 (t, 3 H, 7.6).