is the pyramidality of the nitrogens,[20] clearly disposing the methyl groups to axial and equatorial positions. We assume the nitrogens are more nearly trigonal in **2** by analogy to most phosphonamides,[19] phosphoramides, and 2-oxo-1,3,2-oxazaphosphorinanes unconstrained by small rings.[21]

These structural insights are valuable for the understanding of bonding in these systems and for the rational design of chiral adjuvants. Further studies on the structure and reactivity of P-stabilized anions are in progress.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. S.E.D. acknowledges the A. P. Sloan foundation for a Fellowship (1985–1989). We are also grateful to the National Science Foundation (Presidential Young Investigator Award, NSF CHE-8451321) for support. Dr. Scott R. Wilson and Charlotte Stern are thanked for their help with the X-ray structure analysis.

Supplementary Material Available: A listing of crystal and positional parameters, bond lengths, bond angles, and torsional angles for $[Li^+2^- \cdot 2THF]_2$ (24 pages). Ordering information is given on any current masthead page.

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[20] Sum of the angles: N(1) 346.2°; N(2) 346.4°.

[21] (a) Garcia-Blanco, S.; Perales, A. *Acta Crystallogr., Sect. B* **1972**, *28*, 2647. (b) Brassfield, H. A.; Jacobson, R. A.; Verkade, J. G. *J. Am. Chem. Soc.* **1975**, *97*, 4143. (c) Goodridge, R. J.; Hambley, T. W.; Ridley, D. D. *Aust. J. Chem.* **1986**, *39*, 591. (d) Perales, A.; Garcia-Blanco, S. *Acta Crystallogr., Sect. B* **1977**, *33*, 1935. (e) Bentrude, W. G.; Setzer, W. N.; Sopchik, A. E.; Chandrasekaran, S.; Ashby, M. T. *J. Am. Chem. Soc.* **1988**, *110*, 7119. (f) Denmark, S. E.; Dorow, R. L.; Marlin, J. E. Unpublished X-ray crystal structure analyses.

Diastereoselective Aldol Reactions Using β-Keto Imide Derived Enolates. A Versatile Approach to the Assemblage of Polypropionate Systems

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Received October 2, 1989

We have recently described complementary methods for the synthesis of β-keto imides such as **1** wherein full control of the potentially labile C_2 methyl-bearing stereocenter can be maintained.[1] The surprising attenuation of the kinetic lability of these substrates has been attributed to the intervention of local nonbonding interactions of the A(1,3) type[2] which inhibit the stereoelectronically required alignment of both carbonyls with the C_2 hydrogen. We now describe the unprecedented enolization of this substrate and the diastereoselective aldol reactions of the derived Sn(II) and Ti(IV) enolates which provide access to the complementary diastereomeric β-keto imide adducts **2** and **3** (Scheme I).

Scheme I

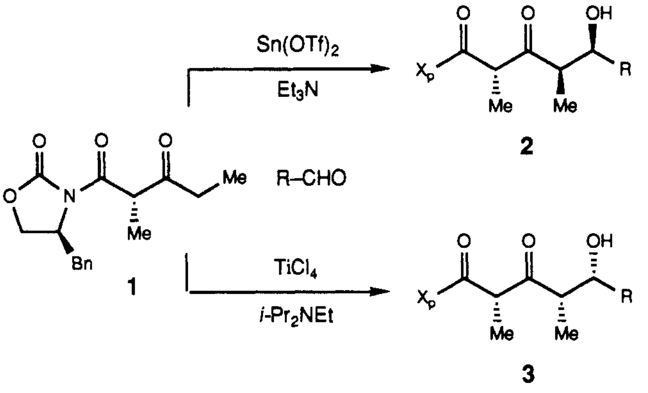
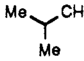
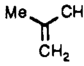
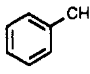


Table I. Aldol Reactions of **1** with Representative Aldehydes (Scheme I)

enolizatn conditns	RCHO[a]	yield,[a] %	ratio[c] **2**:**3**
$Sn(OTf)_2$, Et_3N		83	95:5
$TiCl_4$, iPr_2NEt		86	<1:99
$Sn(OTf)_2$, Et_3N		77[d]	95:5[d]
$TiCl_4$, iPr_2NEt		64[d]	2:98[d]
$Sn(OTf)_2$, Et_3N		71	79:21
$TiCl_4$, iPr_2NEt		86	<1:99
$Sn(OTf)_2$, Et_3N		85	89:11
$TiCl_4$, iPr_2NEt		81	4:96

[a] Unless noted, 1–1.1 equiv of aldehyde was employed in the reaction. [b] Isolated yield of major diastereomer of >99% purity. [c] Ratios determined by HPLC. [d] Yield obtained by using 3–5 equiv of RCHO.

Efforts to effect the regioselective enolization of **1** toward the less substituted ethyl substituent initially focused on the use of Lewis acids in conjunction with tertiary amine bases. After an examination of a number of Lewis acids, it was observed that the Mukaiyama protocol employing $Sn(OTf)_2$[3] with triethylamine (CH_2Cl_2, −20 °C, 1 h) provided a stereochemically homogeneous *Z* enolate which could be trapped by chlorotrimethylsilane.[4] This and related proton quenching experiments established that there is no detectable loss of stereochemistry at C_2 under these enolization conditions. The resultant aldol addition reactions of this enolate proceeded in good yields (71–86%) and stereoselectivities to give the aldol adducts **2** possessing the anti relationship between the C_2 and C_4 methyl groups (Scheme I, Table I).[5] The stereochemical assignments of the aldol adducts **2** and **3** were established by independent unambiguous synthesis. These assignments were confirmed by stereoselective ketone reduction (vide infra) and δ-lactonization to provide substrates from which the four stereocenters could be correlated by ^1H NMR spectroscopy.

In order to amplify the utility of **1** as a dipropionate synthon, we sought to discover other types of metal enolates that might proceed via the complementary aldol reaction to deliver the all-syn aldol diastereomer **3**.[6] This objective was realized when it was

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[1] (a) Evans, D. A. *Aldrichimica Acta* **1982**, *15*, 23–32. These results were previewed in this review (see Scheme XVI). (b) Evans, D. A.; Ennis, M. D.; Le, T.; Mandel, N.; Mandel, G. *J. Am. Chem. Soc.* **1984**, *106*, 1154–1156. Related observations have also been made with our carboximide enolates: (c) DiPardo, R. M.; Bock, M. G. *Tetrahedron Lett.* **1983**, *24*, 4805–4808.

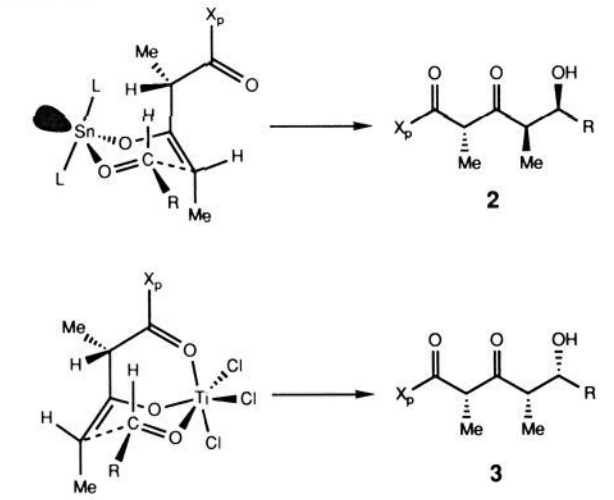
[2] Johnson, F. *Chem. Rev.* **1968**, *68*, 375–413.

[3] Mukaiyama, T.; Iwasawa, N.; Stevens, R. W.; Haga, T. *Tetrahedron* **1984**, *40*, 1381–1390. For a detailed procedure for the synthesis of stannous triflate, see: Evans, D. A.; Weber, A. E. *J. Am. Chem. Soc.* **1986**, *108*, 6757–6761. It is imperative that the reagent must be free of triflic acid, which may be effected by carefully washing the salt with anhydrous ether.

[4] The assignment of the *Z* stereochemistry of this enol ether was made through an unambiguous ^1H NMR NOE study.

[5] General stannous triflate mediated aldol procedure: A magnetically stirred suspension of anhydrous, acid-free $Sn(OTf)_2$ (1.05 equiv, ca. 0.25 M in CH_2Cl_2, +25 °C) is treated with triethylamine (1.05 equiv) and then immediately cooled to −20 °C. (Note: the addition of base sometimes causes the initially white suspension to turn pale yellow.) After 5 min, a solution of the β-keto imide (1.00 equiv, 0.35–0.75 M in CH_2Cl_2) is added dropwise over a 5-min period. The resultant suspension is stirred for 1 h and then cooled to −78 °C prior to treatment with freshly distilled aldehyde (1.00 equiv, neat or in CH_2Cl_2). The reaction mixture is stirred at −78 °C for 30 min and then transferred rapidly by cannula to a cool and vigorously stirred 1:1 mixture of CH_2Cl_2/1 N aqueous $NaHSO_4$ (ca. 130 mL/1 mmol of β-keto imide). After 5–10 min of vigorous stirring at 0 °C, the mixture is diluted with additional 1:1 CH_2Cl_2/1 N aqueous $NaHSO_4$, and the aqueous layer is extracted several times with CH_2Cl_2. The combined organic layers are washed with aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated in vacuo. The product is purified by flash chromatography and/or recrystallization.

Scheme II



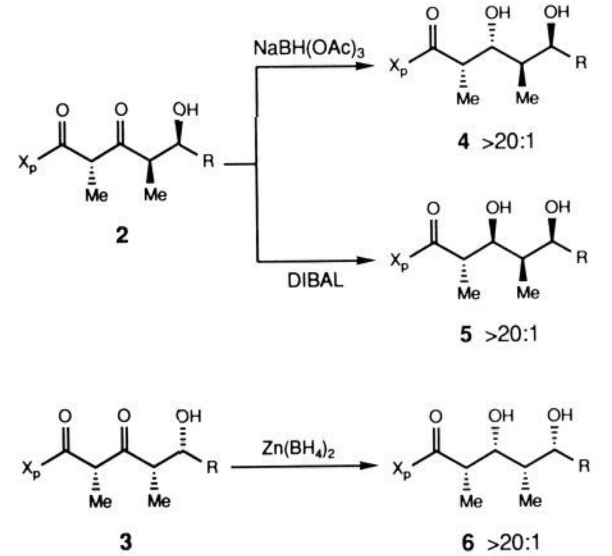
observed that the Z trichlorotitanium enolate derived from **1** provided exceptional levels of asymmetric induction in the aldol addition to give the all-syn adduct **3**.[7] During the course of this study, a highly effective method for the direct generation of these trichlorotitanium enolates was also developed.[8]

In both the Sn(II) and Ti(IV) aldol reactions, ideal 1:1 stoichiometry between enolate and aldehyde can be maintained. Improved yields were noted when excess aldehyde (3–5 equiv) was employed in the aldol reactions of α-methacrolein where competitive aldehyde polymerization was found to be a problem.

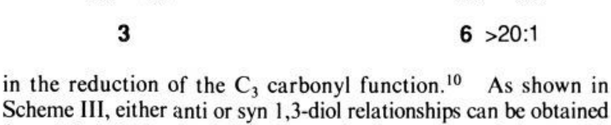
Control experiments indicated that the stereochemical outcome of both reactions is dominated by the C_2 methyl-bearing stereocenter, with the chirality of the oxazolidone auxiliary playing a subordinate but supporting role.[9] For example, in the aldol addition reactions of the two metal enolates derived from **1** with isobutyraldehyde, the Sn(II) and Ti(IV) enolates exhibited 95:5 and <1:99 diastereoselectivities, respectively (Table I). When these same reactions were carried out on an analogue of **1** bearing the enantiomeric chiral auxiliary [4(R)-Bn], the overall sense of asymmetric induction was unaltered but the diastereoselection for both Sn(II) and Ti(IV) enolates diminished to 81:19 and 7:93, respectively. Although little concrete information on the details of chirality transfer is available, the diastereomeric transition states depicted in Scheme II are consistent with the observed stereochemical outcome of the reactions.

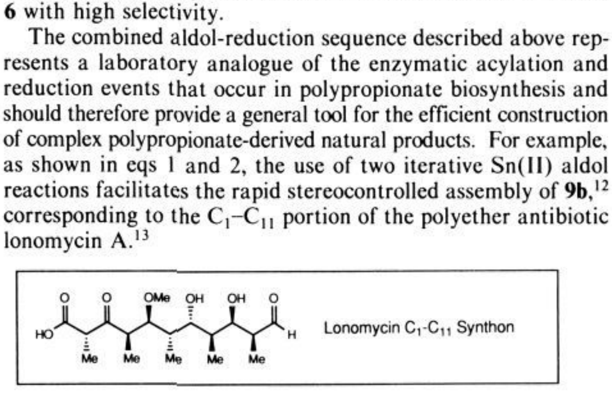
The aldol adducts **2** and **3** were treated with a variety of reducing agents in order to examine the degree of internal direction in the reduction of the C_3 carbonyl function.[10] As shown in Scheme III, either anti or syn 1,3-diol relationships can be obtained from **2** in >20:1 selectivity when reductions are carried out with triacetoxyborohydride[11] or DIBAL, respectively. Selective syn reduction was also performed on aldol adduct **3**, to afford diol **6** with high selectivity.

Scheme III



The combined aldol-reduction sequence described above represents a laboratory analogue of the enzymatic acylation and reduction events that occur in polypropionate biosynthesis and should therefore provide a general tool for the efficient construction of complex polypropionate-derived natural products. For example, as shown in eqs 1 and 2, the use of two iterative Sn(II) aldol reactions facilitates the rapid stereocontrolled assembly of **9b**,[12] corresponding to the C_1–C_{11} portion of the polyether antibiotic lonomycin A.[13]





The details of these investigatons, as well as the application of this method to the asymmetric total synthesis of natural products, will be reported in due course.

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(6) The following metal triflates were examined: manganese triflate, dimethylstannic triflate, dibutylboron triflate, dicyclopentadienylboron triflate, and 9-BBN triflate. We have noted that boron triflates used in conjunction with tertiary amines provide aldol adducts that are identical with those obtained by using titanium tetrachloride and diisopropylethylamine, but in yields and selectivities lower than those obtained with the procedure presented here.

(7) *General titanium tetrachloride mediated aldol procedure:* The β-keto imide **1** is dissolved in dry CH_2Cl_2 (0.25 M) under N_2, and the solution is cooled to −10 °C. $TiCl_4$ (1.1 equiv) is added (as a neat liquid) dropwise, followed by i-Pr_2NEt (1.1 equiv), and the reaction mixture stirred at −10 °C for 1 h. The enolate solution is then cooled to −78 °C, and freshly distilled aldehyde (1.1 equiv) is added dropwise. The reaction mixture is stirred at −78 °C for 30 min and then allowed to come to −40 °C over a 1-h period. Upon warming to 0 °C, the reaction is quenched by the addition of pH 7 buffer (1.6 mL/mmol). After stirring for an additional 5 min at 0 °C, the solution is transferred into CH_2Cl_2 and the product is isolated as described above (footnote 5) for the analogous Sn(II) enolate reactions.

(8) The trichlorotitanium enolate derived from **1** may be generated by precomplexing 1.1 equiv of $TiCl_4$ with **1** (−10 °C, CH_2Cl_2) followed by enolization with diisopropylethylamine. This enolization protocol was based upon related experiments reported by Harrison: Harrison, C. R. *Tetrahedron Lett.* **1987**, *28*, 4135–4138. The generality of this reaction for other substrates will be reported shortly.

(9) Oxazolidinone auxiliaries derived from (S)-valine and (1S,2R)-norephedrine, as well as the parent unsubstituted case, have also been examined, and similar results in reaction diastereoselection have also been observed with these systems.

(10) The following reagents were also examined: lithium tri-*tert*-butoxyaluminum hydride, triisobutylaluminum, L-Selectride, and REDAL.

(11) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560–3578.

(12) Aldehyde **8** was obtained from **2b** by the following sequence: reduction ($NaHB(OAc)_3$, 93%), acetonide formation (2,2-dimethoxypropane, DOWEX-50, 97%), reduction ($LiAlH_4$, 93%), and oxidation (SO_3·py, DMSO, Et_3N, 78%).

(13) (a) Otake, N.; Koenuma, M.; Miyamae, H.; Sato, S.; Saito, Y. *Tetrahedron Lett.* **1975**, 4147–4150. (b) Riche, C.; Pascard-Billy, C. *J. Chem. Soc., Chem. Commun.* **1975**, 951–952.

Acknowledgment. Support has been provided by the National Institutes of Health, the National Science Foundation, and Merck. Postdoctoral fellowships for J.S.C. and R.M. from NATO and V.J.N. and G.S.S. from the NIH are gratefully acknowledged. The NIH BRS Shared Instrumentation Grant Program 1 S10 RR01748-01A1 is acknowledged for providing NMR facilities.

Supplementary Material Available: Experimental procedures and spectral and analytical data for all aldol reaction products (7 pages). Ordering information is given on any current masthead page.

Ring Opening and Oligomerization of Thiirane by Hexaosmium Carbonyl Cluster Complexes

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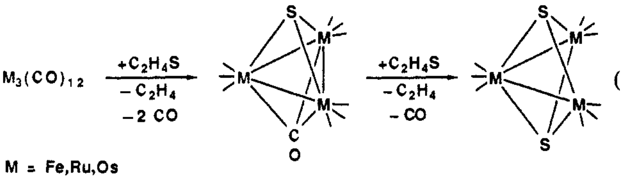
Metal complexes have played central roles in the initiation and propagation of many important polymerization reactions.[1] Studies of the reactions of metal carbonyl cluster complexes with episulfides have shown sulfur transfer and alkene elimination to be the preferred reaction pathway (e.g., eq 1).[2] Although thiirane, C_2H_4S, is able to serve as a ligand through coordination of the sulfur atom,[3] very little is known about the nature of the ring opening and eventual elimination of alkene in these reactions. The desulfurization of thiirane on a clean molybdenum (110) surface is believed to occur by an intramolecular elimination of ethylene without the formation of a thiolate intermediate.[4] We have now investigated the reactions of $Os_6(CO)_{17}(NCMe)$[5] (**1**) and $Os_6(CO)_{16}(NCMe)_2$[5] (**2**) with thiirane and have observed a pattern of ring opening and oligomerization that involves interactions of the metal atoms of the cluster functioning as a group.



(1)

1 (50.7 mg, 0.03 mmol) was allowed to react with 19 μL (0.33 mmol) of $(CH_2)_2S$[6] in 50 mL of CH_2Cl_2 solvent at reflux for 50 min. From this mixture, we have isolated by TLC 6.7 mg of the known compound $Os_6(CO)_{17}(\mu_4\text{-}S)$ (**3**),[7] 13% yield; and 13.8 mg of the new compound $Os_6(CO)_{17}[\mu_3\text{-}S(CH_2)_2S]$ (**4**), 26% yield.[8]

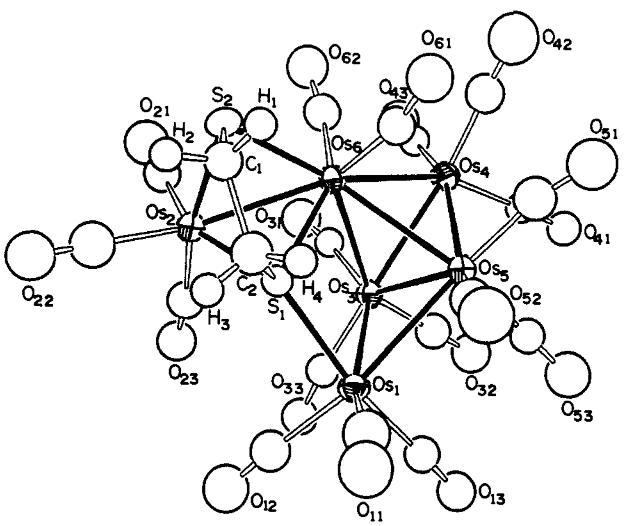


Figure 1. An ORTEP diagram of $Os_6(CO)_{17}[\mu\text{-}S(CH_2)_2S]$ (**4**) showing 50% probability thermal ellipsoids. Selected intramolecular distances (Å) are Os(1)–Os(3) = 2.872 (2), Os(1)–Os(5) = 2.880 (2), Os(2)–Os(6) = 2.814 (2), Os(3)–Os(4) = 2.778 (2), Os(3)–Os(5) = 2.725 (2), Os(3)–Os(6) = 2.897 (2), Os(4)–Os(6) = 2.862, Os(5)–Os(6) = 2.894 (2), Os(1)–S(1) = 2.380 (7), Os(2)–S(1) = 2.353 (7), Os(2)–S(2) = 2.389 (7), Os(6)–S(1) = 2.324 (7), Os(6)–S(2) = 2.401 (7).

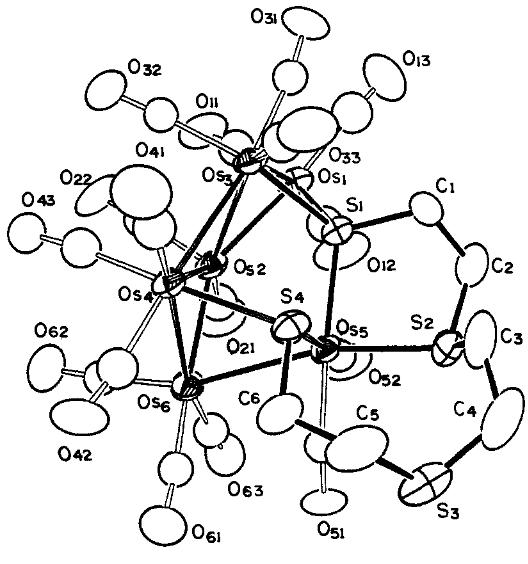


Figure 2. An ORTEP drawing of $Os_6(CO)_{16}[\mu_4\text{-}S(CH_2CH_2S)_3]$ (**7**) showing 50% probability thermal ellipsoids. Selected intramolecular distances (Å) are Os(1)–Os(2) = 2.738 (2), Os(1)–Os(3) = 2.870 (2), Os(2)–Os(3) = 2.767 (1), Os(2)–Os(4) = 2.820 (1), Os(2)–Os(6) = 2.587 (2), Os(3)–Os(4) = 2.980 (2), Os(4)–Os(6) = 2.977 (1), Os(5)–Os(6) = 2.930 (1), Os(5)–S(1) = 2.404 (6), Os(5)–S(2) = 2.432 (6), Os(5)–S(4) = 2.428 (6).

Compound **4** was characterized by IR, ^1H NMR, and single-crystal X-ray diffraction analysis.[9,10] An ORTEP drawing of **4** is shown in Figure 1. Four of the six osmium atoms, Os(3), Os(4), Os(5), and Os(6), are arranged in the shape of a closed tetrahedron. The Os(3)–Os(5) edge of this group is bridged by an $Os(CO)_3$ group, Os(1), and a second $Os(CO)_3$ group, Os(2), is bonded to the cluster at Os(6). An ethanedithiolate group bridges

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[1] (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Chapter 7. (b) Parshall, G. W. *Homogeneous Catalysis*; Wiley: New York, 1980, Chapter 4. (c) Pino, P.; Giannini, U.; Porri, L. Insertion Polymerization In *Encyclopedia of Polymer Science and Engineering*; Wiley: New York, 1987; Vol. 8, pp 147–220.

[2] (a) Adams, R. D.; Babin, J. E.; Tasi, M. *Inorg. Chem.* **1986**, *25*, 4514. (b) Morrow, J. R.; Tonker, T. L.; Templeton, J. L. *Organometallics* **1985**, *4*, 745. (c) Calet, S.; Alper, H. *Tetrahedron Lett.* **1986**, *27*, 3573. (d) Lorenz, I.-P.; Messelauser, J.; Hiller, W.; Conrad, M. *J. Organomet. Chem.* **1986**, *316*, 121. (e) Shunn, R. A.; Fritchie, C. J.; Prewitt, C. T. *Inorg. Chem.* **1966**, *5*, 892. (f) Sander, M. *Chem. Rev.* **1966**, *66*, 297. (g) King, R. B. *Inorg. Chem.* **1963**, *2*, 326. (h) Beck, W.; Danzer, W.; Theil, G. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 582.

[3] Amarasekera, J.; Rauchfuss, R. B.; Wilson, S. R. *J. Am. Chem. Soc.* **1988**, *110*, 2332.

[4] Roberts, J. T.; Friend, C. M. *J. Am. Chem. Soc.* **1987**, *109*, 7899.

[5] Ditzel, E. J.; Holden, D.; Johnson, B. F. G.; Lewis, J.; Saunders, A.; Taylor, M. J. *J. Chem. Soc., Chem. Commun.* **1982**, 1373.

[6] Thiirane was purified by distillation before use and was shown to be pure by ^1H NMR spectroscopy.

[7] Adams, R. D.; Horváth, I. T.; Mathur, P. *Organometallics* **1984**, *3*, 623.

[8] Compound **4** was isolated by TLC on silica gel by elution with a hexane/CH_2Cl_2, 2/1, solvent mixture. For **4**: IR (ν(CO) cm^{-1} in CH_2Cl_2) 2100 (w), 2081 (m), 2067 (vs), 2024 (s, br); ^1H NMR (in CD_3CN) 3.28 (s, br), 3.26 (s, br). Satisfactory elemental analyses for C and H have been obtained.

[9] Dark orange crystals of **4** were grown by slow evaporation of solvent from CH_2Cl_2 solutions at 25 °C, space group, $P2_1/n$, a = 10.101 (2) Å, b = 17.953 (3) Å, c = 16.193 (3) Å, β = 94.75 (1)°, Z = 4. An empirical absorption correction was applied to the data. The structure was solved by direct methods and was refined (2968 reflections) to the final residuals, R = 0.034 and R_w = 0.035.

[10] Diffraction measurements were made on a Rigaku AFC6S diffractometer by using Mo Kα radiation. Calculations were performed on a Digital Equipment Corp. MICROVAX II computer by using the TEXSAN structure solving program library obtained from the Molecular Structure Corp., The Woodlands, TX.

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