(*E*)-**2f**α, 80737-67-3; (*Z*)-**2f**α, 80737-68-4; (*E*)-**2f**β, 80737-69-5; (*Z*)-**2f**β, 80737-70-8; (*E*)-**2f**γ, 80737-71-9; (*Z*)-**2f**γ, 80737-72-0; (*E*)-**2f**δ, 80737-73-1; (*Z*)-**2f**δ, 80737-74-2; (*E*)-**2f**ϵ, 80737-75-3; (*Z*)-**2f**ϵ, 80737-76-4; iodomethane, 74-88-4; dimethyl sulfate, 77-78-1; iodoethane, 75-03-6; 1-iodobutane, 542-69-8; 3-bromo-1-propene, 106-95-6; 3-iodo-1-porpene, 556-56-9; (bromomethyl)benzene, 100-39-0; methyl *trans*-1-butyl-2-phenyl-2-[(trimethylsilyl)oxy]cyclopropanecarboxylate, 80737-77-5; methyl *trans*-2-phenyl-1-(2-propanyl)-2-[(trimethylsilyl)oxy]cyclopropanecarboxylate, 80737-78-6; methyl *trans*-2-phenyl-1-(phenylmethyl)-2-[(trimethylsilyl)oxy]cyclopropanecarboxylate, 80737-79-7.

Asymmetric Alkylation Reactions of Chiral Imide Enolates. A Practical Approach to the Enantioselective Synthesis of α-Substituted Carboxylic Acid Derivatives[1]

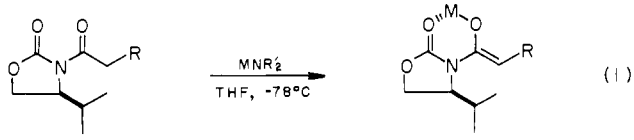
D. A. Evans,* M. D. Ennis, and D. J. Mathre

Contribution No. 6561 from the Laboratories of Chemistry California Institute of Technology Pasadena, California 91125

Received November 23, 1981

The development of chiral enolate synthons and their practical utility in bond construction have been the subject of intensive investigation,[2] and recently several enolate systems have been reported to exhibit high levels of diastereoselection in alkylation reactions.[3] The purpose of this communication is to report our observations on the utility of the enolates derived from *N*-acyl oxazolidones **1** and **2**[4] in complementary diastereoselective alkylation processes (Scheme I). In a recent communication we disclosed the general procedures for the synthesis of imides **1** and **2**, which are readily derived from (1*S*,2*R*)-norephedrine and (*S*)-valinol, respectively.[4,5]

In direct analogy with earlier studies, we have found that either lithium or sodium amide bases (1.1 equiv) [$LiN(i\text{-}C_3H_7)_2$ or $NaN(SiMe_3)_2$, -78 °C, THF] cleanly transform imides **1** and **2** to their respective (*Z*)-metal enolates.[6] From the ensuing results, *enolization stereoselectivity under these conditions must be* >100:1 *(eq 1) if chelated (Z)-enolates such as* **5** *are involved in the*



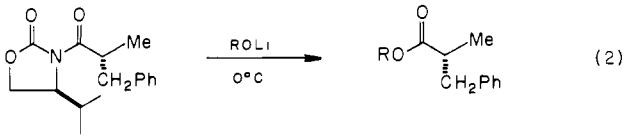
(1)

5a, M = Li

b, M = Na

creation of a diastereofacial bias in the alkylation process. For the alkylation studies summarized in Table I, lithium enolates were employed except for entries K and M-P. General reaction conditions involved treatment of a 0.2-0.5 M solution of the lithium enolate in THF with 3 equiv of alkylating agent at 0 °C (2-4 h).[7] In several instances we have scaled these alkylations up to the 0.3 M level without loss in yield. Diastereomer analysis (**3**:**4**) was carried out by capillary gas chromatography.[8] A number of general trends are evident from the data in the table. First, complementary levels of diastereoface selection can be anticipated from the enolates derived from **1** and **2**, with the latter system exhibiting somewhat greater selectivity. For example, in the reactions of the lithium enolates derived from **1** and **2** with benzyl bromide (entries A, B), the kinetic diastereoselection (**3**:**4**) was found to be 49:1 for **1** (R = Me) and 1:120 for **2** (R = Me), respectively. These data provide an important calibration for the stereoselectivities encountered in *both* the enolization and alkylation processes. Second, we have found that, as anticipated, electrophile structure plays a significant role in dictating reaction stereoselectivity.[3] Qualitatively, "small" alkyl halides are *less* stereoselective than their more sterically demanding counterparts (cf. $PhCH_2Br$ vs. MeI). In general, enolate methylations (entries M-P) with methyl iodide have been the least stereoselective processes encountered to date. In surveying conditions for optimizing this particular process, we have found that alkylation of the sodium enolates (-78 °C) is superior to the analogous reactions of the corresponding lithium enolates (0 °C). One unanticipated benefit encountered in the development of these imide enolate systems has been the ease with which the diastereomeric alkylation products **3** and **4** may be resolved by column chromatography.[9] Overall, the major limitation encountered with the lithium and sodium enolates derived from **1** and **2** is highlighted in entries K and L in the table. One must employ alkylating agents that will react at a convenient rate at temperatures ≤0 °C.[7] The counterpoint to this limitation is the superb diastereoface selection noted for these systems in both alkylations and aldol condensations[4] and the ease with which these chiral oxazolidones may be synthesized and recycled. In all of the alkylation reactions carried out during the course of this study, the sense of asymmetric induction is readily interpreted by assuming a metal-chelated (*Z*)-enolate (see **5**) where diastereoface selection is dictated by the C_4-substituent on the oxazolidone ring.

During the course of this study we have developed a number of useful transformations that nondestructively remove the chiral auxiliaries from the desired chiral synthon. *For example, the alkylated imides may be transformed into benzyl esters with* <0.2% *racemization (eq 2).* The reaction of **6a** (**4**:**3** = 99.9:0.1)[8]



(2)

6a

(*R*)-**7a**, R = CH_2Ph

b, R = H

c, R = CO_2Et

in THF (0.2 M) with $PhCH_2OLi$-$PHCH_2OH$ (prepared from 2.0 equiv of benzyl alcohol and 1.5 equiv of *n*-C_4H_9Li) at 0 °C (1 h) afforded the *R* ester **7a** in 93% yield ($[\alpha]_D$ -26.9° (*c* 6.12, CH_2Cl_2)) along with recovered oxazolidone. Catalytic hydrogenolysis of **7a** afforded (*R*)-**7b** ($[\alpha]_D$ -25.1° (neat) [lit., -25.4° (neat)]).[10] A rigorous racemization assay for this transesterification process was accomplished via the reacylation of the (4*S*)-(2-propyl)oxazolidone with **7c** to give **6a** (**4**:**3** = 99.8:0.2).[8] In more than ten cases that were studied with either chiral aux-

(1) Presented at the 12th International Symposium on the Chemistry of Natural Products, Tenerife, Canary Islands, Evans, D. A.; Takacs, J. M.; McGee, L. R.; Ennis, M. D.; Mathre, D. J.; Bartroli, J. *J. Pure Appl. Chem.* **1981**, *53*, 1109-1127.

(2) For recent reviews see: (a) ApSimon, J. W.; Seguin, R. P. *Tetrahedron* **1979**, *35*, 2797-2842. (b) Meyers, A. I. *J. Pure Appl. Chem.* **1979**, *51*, 1255-1268. (c) Valentine, D., Jr.; Scott, J. W. *Synthesis* **1978**, 329-356.

(3) (a) Evans, D. A.; Takacs, J. M. *Tetrahedron Lett.* **1980**, *21*, 4233-4236. (b) Meyers, A. I.; Yamamoto, Y.; Mihelich, E. D.; Bell, R. A. *J. Org. Chem.* **1980**, *45*, 2792-2796. (c) Schmierer, R.; Grotemeier, G.; Helmchen, G.; Selim, A. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 207-208.

(4) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127-2129.

(5) The optical purities of the oxazolidone chiral auxiliaries employed in this study were determined to be >99% by GLC analysis of the imides derived from the Mosher acid chloride: Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543-2549.

(6) The assignment of the (*Z*)-enolate geometry to these systems has not been rigorously established; however, it is fully consistent with an interpretation of the results obtained in this and related studies (see ref 3a, 4).

(7) At temperatures >0 °C the lithium enolates will decompose via a ketene pathway. The corresponding sodium enolates exhibit reasonable stability at <-20 °C.

(8) Gas chromatographic analyses employed a Hewlett-Packard instrument (Model 5880A) and 30 m × 0.32 mm WCOT columns (column types: Carbowax 20 M, methyl silicone, SE-54, DB-1).

(9) Diastereomer resolution was carried out either by medium-pressure chromatography using Merck Lobar silica gel columns or by the flash method: Still, W. C.; Kahn, M.; Miltra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.

(10) Helmchen, G.; Nill, G.; Flockerzi, D.; Youssef, M. S. K. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 63-65.

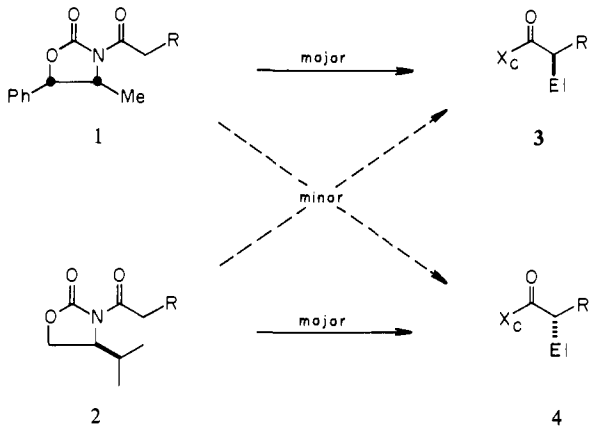
0002-7863/82/1504-1737$01.25/0

Table I. Stereoselective Alkylations of the Enolates Derived from Imides 1 and 2 (Scheme I)

entry	imide	electrophilic (El^+)	kinetic ratio (3:4)[a]	purified ratio (3:4)[b]	isolated yield, %[c]	$[\alpha]_{589}$ (c, CH_2Cl_2),[d] deg	mp (bp), °C
A	1 (R = Me)	$PhCH_2Br$	98:2	>99:1	78	+78.5 (1.68)	(150)[h]
B	2 (R = Me)	$PhCH_2Br$	<1:99	<1:99	92	+9.42 (2.06)	liquid[g]
C	1 (R = Me)	CH_2=C(Me)CH_2I	97:3	>99:1	73	+33.7 (5.9)	42-44
D	2 (R = Me)	CH_2=C(Me)CH_2Br	2:98	<1:99	62	+71.4 (1.79)	liquid[g]
E	1 (R = Me)	CH_2=$CHCH_2Br$	98:2	>99:1	75	+47.0 (2.36)	69-70
F	2 (R = Me)	CH_2=$CHCH_2Br$	2:98	<1:99	71	+62.9 (3.48)	liquid[g]
G	1 (R = Me)	$PhCH_2OCH_2Br$[e]	98:2	>99:1	72	+37.0 (2.07)	(180)[h]
H	2 (R = Me)	$PhCH_2OCH_2Br$[e]	2:98	1:99	77	+35.4 (2.88)	(180)[h]
I	1 (R = Me)	EtO_2CH_2Br	93:7	99:1	51	+35.7 (1.78)	(160)[h]
J	2 (R = Me)	EtO_2CH_2I	5:95	<1:99	51	+48.7 (1.64)	(150)[h]
K	1 (R = Me)	EtI	88:12 (94:6)	>99:1	53[f]	+54.7 (1.38)	71-72
L	2 (R = Me)	EtI	6:94	<1:99	36	+61.6 (0.85)	liquid[g]
M	1 (R = Et)	MeI	87:13 (93:7)	>99:1	82[f]	+6.1 (1.72)	65-66
N	2 (R = Et)	MeI	11:89 (9:91)	1:99	79[f]	+112.6 (4.1)	(180)[i]
O	1 (R = n-C_8H_{17})	MeI	89:11 (94:6)	>99:1	70	-1.41 (1.56)	42-43
P	2 (R = n-C_8H_{17})	MeI	9:91 (7:93)	<1:99	77[f]	+83.3 (2.03)	(160)[j]

[a] Ratios determined by capillary GLC (ref 8); values obtained from the lithium enolates (THF, 0 °C); values in parentheses are for alkylations carried out on the sodium enolates (THF, −78 °C). [b] See ref 9. [c] In all cases, the yields are reported on chromatographed material whose diastereomer composition is noted in preceeding column. [d] All rotations were determined in methylene chloride (c = g/100 mL). [e] Reaction carried out at −40 °C with 3 equiv of alkyl bromide. [f] Preparative experiment carried out on the sodium enolate (−78 °C) with 5 equiv of methyl iodide. [g] In these instances analytically pure samples were prepared by high-vacuum solvent removal. [h] 5×10^{-3} mm. [i] 0.01 mm. [j] 8×10^{-3} mm.

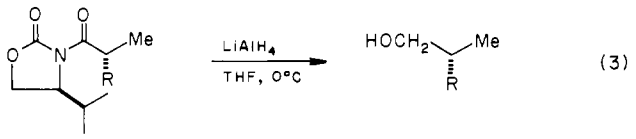
Scheme I[a]



[a] Conditions: (a) MNR_2; (b) El^+.

iliary, efficient transesterification was noted in yields in excess of 90%.

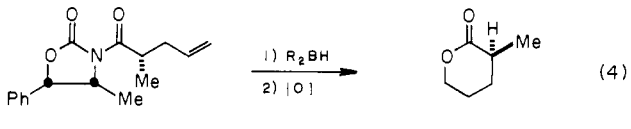
We have also observed that primary alcohols can be obtained by reduction of these imides with either lithium aluminum hydride or lithium borohydride (eq 3). As a representative procedure,



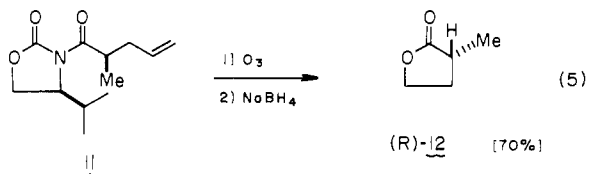
(3)

treatment of a 0.2–0.4 M solution of **6a** (**4**:**3** > 99:1) with 3 molar equiv of $LiAlH_4$ (0 °C, 0.5–2 h) afforded an 86% isolated yield of R alcohol **8a** ($[\alpha]_D$ +11.0° (c 1.15, C_6H_6) [lit. for (S)-**8a**, −11.08° (c 4.6, C_6H_6)][11]) along with the *unreduced* oxazolidone chiral auxiliary. In a similar fashion **6b** and **6c** (**4**:**3** > 99:1) were respectively reduced to the S alcohol **8b** ($[\alpha]_D$ = +5.3° (c 2.2, EtOH) [lit. +4.97° (c 0.9, EtOH)][12]) and (R)-2-methyldecanol, **8c** ($[\alpha]_D$ = −10.0° (c 4.2, CH_2Cl_2) [lit. −9.8° (neat)][13]) in ≥85% yield. It is noteworthy that the chiral synthon (R)-**8** and its enantiomer (S)-**8** can be prepared from **2** (R = Me) and **1** (R = Me), respectively, in two steps in overall yields of 55–60%.

Additional chemical operations that both establish the sense of asymmetric induction in the alkylation process and provide information as to the tolerance of these imides to oxidants are illustrated below in eq 4 and 5. Hydroboration of **9** (1.1 equiv



(4)



(5)

of $(Sia)_2BH$, THF, 0 °C, 2 h) followed by oxidation and lactonization afforded lactone (S)-**10** ($[\alpha]_D$ = +67.3° (c 6.59, MeOH)) in good agreement with calculated rotations ($[\alpha]_D$ = −58.1°, −64.4°) for the (R)-enantiomer.[3b] Alternatively, **11** was ozonized (−78 °C, MeOH)[14] and the resultant aldehyde reduced with sodium borohydride[15] to the carbinol, which spontaneously lactonized to (R)-**12** upon distillation ($[\alpha]_D$ = +21.2° (c 8.6, EtOH)). This value is again in good agreement with the highest literature value [+23.1° (c 9.7, EtOH)] reported for this lactone.[10]

Acknowledgment. This research was supported by the National Science Foundation (Grant CHE-81-01742) and the National Institutes of Health (Grant CA-28187). We also acknowledge the use of the Southern California Regional NMR Facility (Grant NSF-7916324A1).

Registry No. 1 (R = Me), 77877-20-4; **1** (R = Et), 80697-91-2; **1** (R = n-C_8H_{17}), 80697-92-3; **2** (R = Me), 77877-19-1; **2** (R = Et), 80697-93-4; **2** (R = n-C_8H_{17}), 80719-69-3; **3** (R = Me; E = CH_2—Ph),

(11) (a) Terashima, S.; Yamada, S.-I. *Chem. Pharm. Bull.* **1968**, *16*, 1953–1971. (b) Wiberg, K. B.; Hutton, T. W. *J. Am. Chem. Soc.* **1956**, *78*, 1640–1645. These authors report a rotation of +11.83° (neat).

(12) Branca, Q.; Fischli, A. *Helv. Chim. Acta* **1977**, *60*, 925–944.

(13) Byström, S.; Högberg, H.-E.; Norin, T. *Tetrahedron* **1981**, *37*, 2249–2254.

(14) Veysoglu, T.; Mitscher, L. A.; Swayze, J. K. *Synthesis* **1980**, 807–810.

(15) Santaniello, E.; Ponti, F.; Manzocchi; A. *Synthesis* **1978**, 891–892.

(16) Satisfactory elemental analyses and spectral data were obtained for all compounds reported herein.

80697-94-5; **3** (R = Me; E = CH_2—C(Me)=CH_2), 80719-70-6; **3** (R = Me; E = CH_2—CH=CH_2), 80697-95-6; **3** (R = Me; E = CH_2—O—CH_2—Ph), 80697-96-7; **3** (R = Me; E = CH_2—O—O—Et), 80697-97-8; **3** (R = Me; E = Et), 79563-30-7; **3** (R = Et; E = Me), 79563-31-8; **3** (R = n-C_8H_{17}; E = Me), 80697-98-9; **4** (R = Me; E = CH_2—Ph), 79563-27-2; **4** (R = Me; E = CH_2—C(Me)=CH_2), 79563-28-3; **4** (R = Me; E = CH_2—CH=CH_2), 79563-29-4; **4** (R = Me; E = CH_2—O—CH_2—Ph), 80697-99-0; **4** (R = Me; E = CH_2—O—O—Et), 80719-71-7; **4** (R = Me; E = Et), 80735-97-3; **4** (R = Et; E = Me), 80735-98-4; **4** (R = n-C_8H_{17}; E = Me), 80698-00-6; **5a** (R = Me), 80698-01-7; **5a** (R = Et), 80698-02-8; **5a** (R = n-C_8H_{17}), 80698-03-9; **5b** (R = Me), 80698-04-0; **5b** (R = Et), 80698-05-1; **5b** (R = n-C_8H_{17}), 80698-06-2; **6a**, 79563-27-2; **6c**, 80698-11-9; (*R*)-**7a**, 80698-12-0; (*R*)-**7b**, 14367-67-0; (*R*)-**7c**, 80698-13-1; (*R*)-**8a**, 77943-96-5; (*S*)-**8b**, 63930-46-1; (*R*)-**8c**, 80698-14-2; **9**, 80764-26-7; (*S*)-**10**, 80698-15-3; **11**, 79563-29-4; (*R*)-12, 55254-35-8; $PhCH_2Br$, 100-39-0; CH_2=C(Me)-CH_2I, 3756-30-7; CH_2=C(Me)CH_2Br, 1458-98-6; CH_2=$CHCH_2Br$, 106-95-6; $PhCH_2OCH_2Br$, 17690-16-3; EtO_2CH_2Br, 80698-16-4; EtO_2CH_2I, 80698-17-5; EtI, 75-03-6; MeI, 74-88-4; (4*S*)-(2-propyl)oxazolidone, 17016-83-0.

Preparation and Structure of Tungsten Neopentylidene Hydride, Neopentylidene Carbonyl, and Neopentylidene Ethylene Complexes[1]

J. H. Wengrovius, R. R. Schrock,*† M. R. Churchill,*‡ and H. J. Wasserman

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
and Department of Chemistry
State University of New York
Buffalo, New York 14214

Received November 16, 1981

We have found that tungsten alkylidene complexes are especially stable when a strong π donor such as an oxo[2] or imido[3] ligand is present and that a neopentylidene ligand in two such species[4] is less distorted than any we have encountered in tantalum or niobium chemistry.[5] We also know that oxo and imido alkylidene complexes are olefin metathesis catalysts.[3,4a,6] An important question is what the structure and reactivity of tungsten alkylidene complexes will be when no strong π-donor ligand is present. We report three examples of such species here. These results along with recent results concerning the structure of analogous methylene complexes[7] and the formation of W(VI) neopentylidyne complexes[8] reinforce the notion that tungsten alkylidene ligands are likely to be highly distorted in the absence of a strong π-donor ligand and, when the electron count is less than 18, may form an alkylidyne ligand by loss of an α proton.

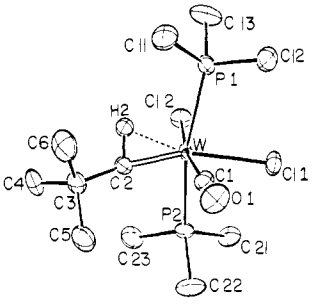


Figure 1. Overall geometry of the $W(CHCMe_3)(CO)Cl_2(PMe_3)_2$ molecule. Hydrogen atoms of the methyl groups are omitted for clarity.

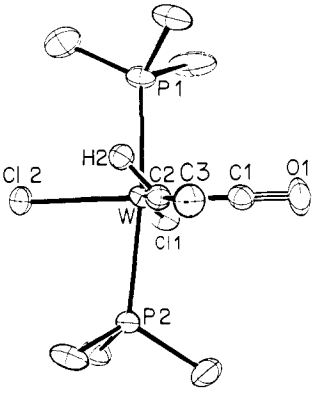
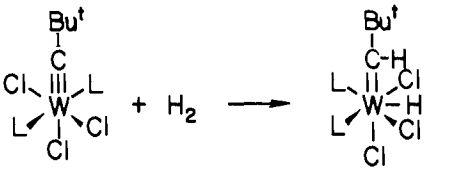


Figure 2. $W(CHCMe_3)(CO)Cl_2(PMe_3)_2$ molecule, showing the orientation of the α-hydrogen atom (H2) relative to the P1···Cl2···C2 octahedral face.

Yellow $W(CCMe_3)Cl_3L_2$[9] (L = PMe_3) reacts with molecular hydrogen (30 psi, 12 h, CH_2Cl_2) to give pale yellow $W(CHCMe_3)(H)Cl_3L_2$[10] (**1**, eq 1). The pentagonal bipyramidal



(1)

1

structure is suggested by the fact that only a single type of phosphine ligand is present, by the large coupling of the hydride to phosphorus (78 Hz), and by comparison with the structure of $Ta(CCMe_3)(H)(dmpe)_2(ClAlMe_3)$ (dmpe = bis(dimethylphosphino)ethane).[5a] The neopentylidene ligand is highly distorted, as judged by a low value for J_{CH_α} (84 Hz) and ν_{CH_α} (2395 cm^{-1}) and the relatively high-field chemical shift of H_α (1.35 ppm).

Although the spectra of **1** do not change down to −60 °C, the neopentylidene ligand in **1** is likely to be rotating rapidly on the NMR time scale (i.e., H_α is not localized) as found in other complexes such as $Ta(CHCMe_3)(PMe_3)_4Cl$,[11] which contain grossly distorted neopentylidene ligands. $W(CHCMe_3)(H)Cl_3L_2$ is the first example of an alkylidene hydride complex of tungsten(VI).[12]

† Massachusetts Institute of Technology.
‡ State University of New York.

(1) Multiple Metal–Carbon Bonds. 25. For part 24 see ref 5a.
(2) Wengrovius, J. H.; Schrock, R. R. *Organometallics* **1982**, *1*, 148.
(3) Pedersen, S., unpublished results.
(4) (a) Churchill, M. R.; Rheingold, A. L.; Youngs, W. J.; Schrock, R. R.; Wengrovius, J. H. *J. Organomet. Chem.* **1980**, *204*, C17. (b) Churchill, M. R.; Missert, J. R.; Youngs, W. J. *Inorg. Chem.* **1981**, *20*, 3388.
(5) (a) Churchill, M. R.; Wasserman, H. J.; Turner, H. W.; Schrock, R. R. *J. Am. Chem. Soc.*, this issue. (b) Churchill, M. R.; Wasserman, H. J. *Inorg. Chem.* **1981**, *20*, 2899. (c) Churchill, M. R.; Hollander, F. J. *Inorg. Chem.* **1978**, *17*, 1957. (d) Churchill, M. R.; Youngs, W. J. *Inorg. Chem.* **1979**, *18*, 1930. (e) Schultz, A. J.; Brown, R. K.; Williams, J. M.; Schrock, R. R. *J. Am. Chem. Soc.* **1981**, *103*, 169.
(6) Schrock, R.; Rocklage, S.; Wengrovius, J.; Rupprecht, G.; Fellmann, J. *J. Mol. Catal.* **1980**, *8*, 73–83.
(7) Holmes, S. J.; Schrock, R. R. *J. Am. Chem. Soc.* **1981**, *103*, 4599–4600.
(8) Wengrovius, J. H.; Sancho, J.; Schrock, R. R. *J. Am. Chem. Soc.* **1981**, *103*, 3932.
(9) Prepared by treating $W(CCMe_3)Cl_3(PMe_3)_3$[8] with C_2Cl_6 in CH_2Cl_2. $[Et_3PCl]Cl$ was filtered off and the residue that remained after removing all volatiles was recrystallized from ether/pentane; yield 85%. δ C_α ($CDCl_3$) = 357 (t, $^2J_{CP}$ = 26 Hz).
(10) Anal. Calcd for $WC_{11}H_{29}Cl_3P_2$: C, 25.73; H, 5.69. Found: C, 26.13; H, 5.95. δ_{C_α} ($CDCl_3$) = 236 (dt, J_{CH} = 84 Hz, $^2J_{CP}$ = 19 Hz, J_{CW} = 87 Hz); δ_{H_α} = 1.35 (dt, $^3J_{HH}$ = 1 Hz, $^3J_{HP}$ = 2 Hz); δ_{WH} = 9.88 (dt, $^3J_{HH}$ = 1 Hz, $^2J_{HP}$ = 78 Hz, J_{HW} = 16 Hz); δ_P = −1.07 (d, $^2J_{PH}$ = 82 Hz, J_{PW} = 142 Hz); ν_{CH_α} = 2395 cm^{-1}, ν_{WH} = 1999 cm^{-1}.
(11) Fellmann, J. D.; Turner, H. W.; Schrock, R. R. *J. Am. Chem. Soc.* **1980**, *102*, 6609.
(12) Related tantalum complexes such as $Ta(CHCMe_3)(H)Cl_2(PMe_3)_3$ have been reported recently.[11]

0002-7863/82/1504-1739$01.25/0