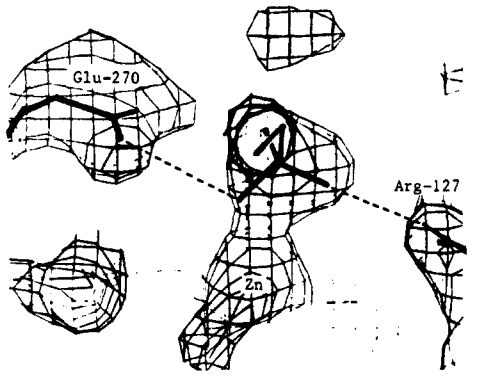


Figure 1. Portion of a $(5|F_o| - 4|F_c|)$ difference electron density map looking into the hydrophobic pocket of CPA. The bound phosphonate and phenylalanine moieties (ca. 60% occupancy), as well as the side chains of Glu-270 and Arg-127, were omitted from the structure factor calculation in order to obtain an unbiased map. Glu-270, the tetrahedral phosphonate above zinc, and the guanidinium moiety of Arg-127 are visible. The carboxylate group of the bound phenylalanine in the S_1' subsite is just visible in the upper background. Possible hydrogen bonds are denoted as dashed lines.

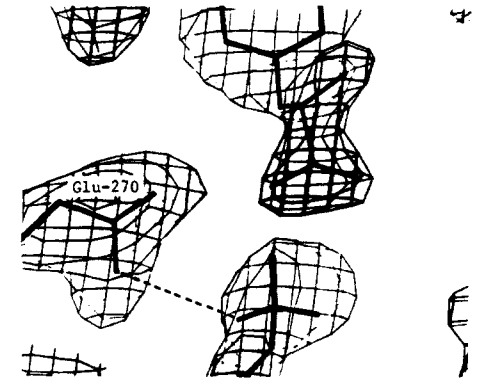


Figure 2. Same map as Figure 1, but viewed from a different angle. Note the relative positions of phosphonate and phenylalanine. Major reorientation occurred around the phenylalanine C_α–C_β and C_β–C_γ bonds in this observed conformation.

participation of zinc, at certain steps in substrate hydrolysis regardless of mechanism (promoted water/hydroxide or anhydride).

The phenylalanine bound in the S_1' subsite makes no hydrogen bond contacts with the enzyme. One oxygen of its carboxylate moiety, however, is within hydrogen bonding distance (2.7 Å) to a third phosphonate oxygen (i.e., the one not interacting with Glu-270 or Arg-127), yet it is in poor geometric orientation. Additionally, the molecule has endured significant rotations about C_α–C_β and C_β–C_γ (Figure 2) so that the amino nitrogen is directed out toward solution and the carboxylate has severed its salt link with Arg-145. The molecule may be tending toward a carboxyl-carboxylate interaction with Glu-270, similar to that observed in the product complex of CPA with the cleaved potato inhibitor (with C-terminal Gly),[8] yet is restrained by both the bulky phenyl group in the hydrophobic pocket of the enzyme and the three oxygens of the tetrahedral phosphonate. The observed orientation of phenylalanine may represent some step of product release,[9] which could occur through a carboxyl–carboxylate interaction with Glu-270. If, however, the observed orientation is merely the result of additional interactions provided by the tetrahedral phosphonate, the orientation of phenylalanine may be a nonproductive consequence.

It is uncertain whether CPA has actually participated in the cleavage of the phosphonamidate linkage in the crystal, but kinetic studies[4] in solution revealed no such effect. The reported[4] purity of synthetic inhibitor is about 86%; presumable contaminants are the hydrolyzed phosphonamidate moieties, neither of which bind to CPA with an affinity anywhere near that of the phosphonamidate itself ($K_i = 9.0 \times 10^{-8}$ M at pH 7.5). Except for travel time via the US mail, the inhibitor was stored at 4 °C, and all crystal chemistry, except data collection, was performed at 4 °C at pH 7.5. These are conditions that do not favor the immediate hydrolysis of the phosphonamidate, and at this pH at room temperature it has a reported[4] half-life of more than 8 days; certainly the lower temperature would only serve to increase its lifetime (at pH 8.5 at 4 °C it is reported to be indefinitely stable in stock solutions). It could well be that during the span of crystallographic data collection at room temperature (about 8 days), the bound phosphonamidate hydrolyzed enough, with or without the participation of the enzyme, to make the crystallographically observed time-averaged structure a cleaved inhibitor. Further study of this system at lower temperature and slightly higher pH may yield the structure of an intact complex.[10]

(9) The conformation of Tyr-248, a residue implicated in substrate binding, is disordered in the electron density maps, although the more continuous density puts it in the so-called "up" position. Such a conformation favors product release, since in this position Tyr-248 does not cover the active site.

(10) We thank Prof. Paul A. Bartlett for generously supplying us with ZGP'. Additionally, we acknowledge the National Institutes of Health for Grant GM 06920 in support of this research and the National Science Foundation for Grant PCM-77-11398 in support of the computational facility. D.W.C. thanks AT&T Bell Laboratories for a doctoral fellowship.

Photochemistry of *p*-Nitrophenyl Azide: Single-Electron-Transfer Reaction of the Triplet Nitrene

Tsuei-Yun Liang and Gary B. Schuster*

Department of Chemistry, Roger Adams Laboratory
University of Illinois, Urbana, Illinois 61801

Received May 20, 1985

Aromatic azides, nitro-substituted phenyl azides in particular, find widespread use as photolabeling agents of biological macromolecules.[1] In this report we describe the photochemistry of *p*-nitrophenyl azide (**1**).[2,3] Irradiation of **1** leads to loss of nitrogen and formation of (*p*-nitrophenyl)nitrene (**3**). Our findings reveal that the reaction of this triplet nitrene with tertiary amines proceeds by a single-electron-transfer (SET) route not by the hydrogen abstraction pathway generally associated with nitrenes.[3]

Photolysis of azide **1** at 77 K generates a transient species that exhibits an absorption maximum at ca. 375 nm. This absorption has previously been assigned[4] to triplet nitrene **3** on the basis of an EPR spectrum.[5] Irradiation of a 4.8×10^{-4} M solution of azide **1** in benzene (or chlorobenzene or benzonitrile) at room temperature with the output of a nitrogen laser[6] (15 ns, 337 nm, 7.0 mJ) creates a similarly adsorbing transient product. This species is generated within the rise time of the laser pulse and leads to formation of 4,4'-dinitroazaobenzene (**6**) by a second-order process with a rate constant of 1×10^9 M^{-1} s^{-1}. The yield of azobenzene **6** at low conversion is nearly quantitative. These observations assist in the assignment of the observed transient species to triplet nitrene **3**.

(1) Chowdry, V.; Westheimer, F. H. *Annu. Rev. Biochem.* **1979**, *48*, 293. Knowles, J. R. *Acc. Chem. Res.* **1972**, *5*, 155. Bayley, H. "Laboratory Techniques in Biochemistry and Molecular Biology"; Work, Burdon, Eds.; Elsevier: amsterdam, 1983.

(2) The photochemistry of this azide has been examined previously in inert solvents. Nakayma, H.; Nozawa, M.; Kanaoka, Y. *Chem. Pharm. Bull.* **1979**, *27*, 2775.

(3) For reviews of azide photochemistry, see: Scriven, E. F. V. In "Reactive Intermediates"; Abramovitch, R. A., Ed.; Plenum Press: New York, 1982; Vol. 2, and references cited therein.

(4) Smirnov, V. A.; Brichkin, S. B. *Chem. Phys. Lett.* **1982**, *87*, 548.

(5) Wasserman, E. *Prog. Phys. Org. Chem.* **1971**, *8*, 319. Hall, J. H.; Fargher, J. M.; Matthias, R. G. *J. Am. Chem. Soc.* **1978**, *100*, 2029.

(6) The laser spectrometer has been described previously. Horn, K. A.; Schuster, G. B. *Tetrahedron* **1982**, *38*, 1095.

0002-7863/86/1508-0546$01.50/0

Scheme I

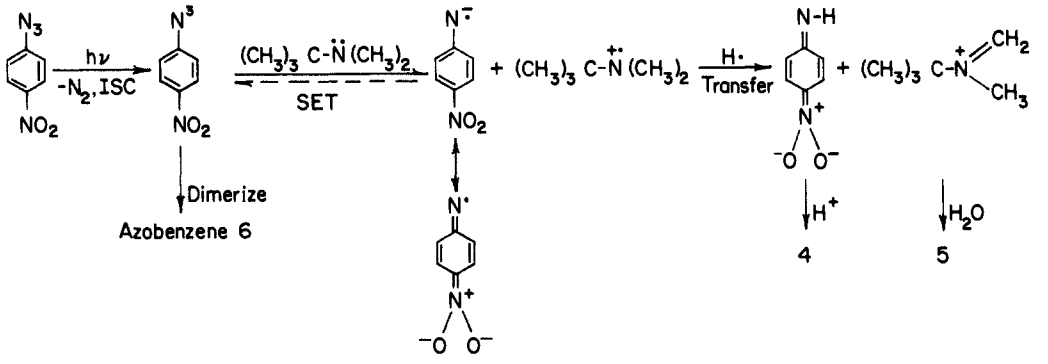
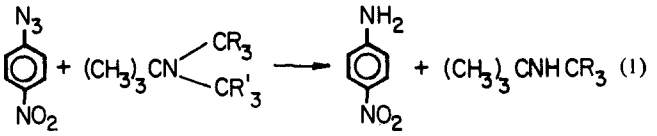


Table I. Photolysis of *p*-Nitrophenyl Azide with *tert*-Butyldimethylamine

solvent	amine[a]	light source	yields[b] 6	4	5	5a,b
PhCl	**2a**	continuous	39	20	35	
PhCl	**2a**	laser	100	1	1	
PhCN	**2a**	continuous	51	42	30	
PhCN	**2b**	continuous				3.3 ± 0.2
PhCN	**2a** + **2c**	continuous				1.5 ± 0.1

[a] The concentration of amine is 0.5 M and that of azide **1** is 1×10^{-2} M. [b] Yields are based on consumed azide **1** which is kept in all cases below 40%.

Irradiation of azide **1** in benzonitrile containing 0.5 M *tert*-butyldimethylamine with a continuous, low-power light source[7] gives, in addition to azobenzene **6**, *p*-nitroaniline (**4**) and *tert*-butylmethylamine (**5**) from the oxidative demethylation of the starting amine,[8] see Table I and eq 1. These products result from



1 **2a**; R=R'=H **2b**; R=H, R'=D **2c**; R=R'=D 4 **5a**; R=H **5b**; R=D

the reaction of an intermediate formed from irradiation of the azide with the tertiary amine. Traditionally, this key intermediate has been identified as the triplet nitrene and the first step in the reaction sequence is formulated as hydrogen atom abstraction.[2,3,9] Alternatively, the intermediate initiating these reactions might be the electronically excited azide. Reaction of electronically excited nitroaromatic compounds with amines is well-known.[10] Also, it is reasonable to expect that the first step in the reaction sequence could be electron transfer from the amine to either the nitrene or to the electronically excited azide. We performed a series of experiments to test these possibilities.

Reaction originating with the excited azide or singlet nitrene may be distinguished from one that proceeds from the triplet nitrene by examining the power dependence of photolysis of **1** in the presence of the amine. It is clear from the kinetic results described above that azobenzene **6** is formed by dimerization of the triplet nitrene. If aniline **4** and amine **5** result primarily from reaction of excited azide (or singlet nitrene), then the power of the light source should not influence either the ratio of **6** to **4** or of **6** to **5**. In contrast, if the triplet nitrene is the origin of aniline **4** and amine **5** as well as of azobenzene **6**, then the yield of **6** should increase compared to **4** and **5** when the power of the light source increases. Irradiation of azide **1** in the presence of amine **2a** with the laser instead of the continuous, low-power lamp (ca. 20000-fold higher intensity with the laser) gives essentially a quantitative yield of azobenzene **6** (Table I). This finding clearly supports schemes where all bimolecular reactions begin with the triplet nitrene.

Reactions initiated by electron transfer can be distinguished from those that proceed by rate-limiting hydrogen atom abstraction by analysis of product isotope effects.[10] In particular, if hydrogen atom abstraction is the key step, then *tert*-butyldimethylamine-d_3 (**2b**) will exhibit approximately the same isotope effect as a 1:1 mixture of *tert*-butyldimethylamine-d_0 (**2a**) and *tert*-butyldimethylamine-d_6 (**2c**). In contrast, if electron transfer is the product-determining step, then amine **2b** can exhibit an isotope effect considerably larger than that of a 1:1 mixture of the amines **2a** and **2c**.[11]

The *tert*-butylmethylamine (**5a,b**) formed by irradiation of azide **1** in solutions containing *tert*-butyldimethylamine was analyzed for deuterium content by chemical ionization mass spectroscopy. The findings (Table I) form a pattern that signal the inclusion of an electron-transfer step in the reaction mechanism. The isotope effect obtained for the d_3 amine **2b** is more than twice that for the mixture of d_0 and d_6 amines **2a,c**. If electron transfer is irreversible and uniquely responsible for demethylation of **2**, then no isotope effect is expected from the mixture of d_0 and d_6 amines. The small isotope effect observed in this experiment is not surprising. Related observations have been explained by suggesting that the electron transfer is reversible[12] or that the "hole" on the tertiary amine hops from one amine to another in competition with deprotonation.

The reaction sequence for photolysis of *p*-nitrophenyl azide supported by our results is shown in Scheme I. Excitation generates the singlet excited azide that rapidly loses N_2 to form the singlet nitrene which intersystem crosses to the detected triplet nitrene. Triplet (*p*-nitrophenyl)nitrene may dimerize to form the azo compound, or, in the presence of a tertiary amine, be reduced to the nitrene radical anion. Nitrene radical anions have been observed previously in the gas phase.[14] Stabilization of this species by resonance with the 4-nitro substituent may in this case influence the selection of this path. Eventual hydrogen transfer, perhaps primarily within the initial solvent cage, forms the even-electron intermediates that lead to *p*-nitroaniline and, after hydrolysis,[8]

(7) The light source is an Oriel 200 W Xe/Hg resonance lamp filtered through an 8-cm path-length solution of K_2CrO_4 in water. This filter transmits light from 295 to 330 nm. These wavelengths are absorbed nearly exclusively by azide **1** when its conversion to products is kept below 50%.

(8) Demethylation of amines following oxidation is a well-known process that involves hydrolysis of an intermediate iminium ion by trace amounts of water: Cohen, S. G.; Parola, A.; Parsons, G. H. *Chem. Rev.* **1973**, *73*, 141.

(9) Abramovitch, R. A.; Challand, S. R. *J. Chem. Soc., Chem. Commun.* **1972**, 964.

(10) Dopp, D.; Heufer, J. *Tetrahedron Lett.* **1982**, 1553.

(11) Amine **2b** (86.4% CD_3) was prepared from *tert*-butylmethylamine-d_3, formaldehyde, and formic acid according to: Icke, R. N.; Wisegarver, R. B. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. 3, p 723. Amine **2c** (99% d_6) was prepared from *tert*-butylamine and methyl iodide-d_3.

(12) Inbar, S.; Linschitz, H.; Cohen, S. G. *J. Am. Chem. Soc.* **1980**, *102*, 1419; **1981**, *103*, 1048.

(13) Schrock, A. K.; Schuster, G. B. *J. Am. Chem. Soc.* **1984**, *106*, 5228 and references cited therein.

(14) McDonald, R. N.; Chowdhury, A. K. *J. Am. Chem. Soc.* **1983**, *105*, 198.

(15) After this report was submitted, Tomioka and co-workers reported a related investigation of electron transfer during photolysis of nitrophenyldiazomethane. Tomioka, H.; Tabayshi, K.; Izawa, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 907. See also: Goh, S. H.; Gian, L. H. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1625.

tert-butylmethylamine. These results are the first indication that single electron transfer plays a role in the chemistry of aryl nitrenes.[15]

Acknowledgment. We thank specially Carter Cook and Richard Milberg of this Department for their assistance with the mass spectrometric analysis of *tert*-butylmethylamine. This work was supported by the National Institutes of Health.

Oxidative Transformation of Monobromotetracarbonyl(alkylidyne) Complexes of Molybdenum and Tungsten into Tribromo(alkylidyne) Complexes

Andreas Mayr* and Gregory A. McDermott

Department of Chemistry, Princeton University
Princeton, New Jersey 08544

Received November 5, 1985

The chemistry of alkylidyne, or carbyne, complexes of molybdenum and tungsten in high oxidation states has been developed during the past years by Schrock and co-workers. This work has led to the discovery of remarkable reactions such as acetylene metathesis by trisalkoxymetalalkylidyne complexes of tungsten[1] and molybdenum[2] or the formation of cyclopentadienyl ligands in the reaction of trihalotungsten alkylidyne complexes with acetylenes.[3] Most of this chemistry was investigated by using neopentylidyne systems. This restriction originates in the synthetic method used for the preparation of the alkylidyne complexes, α-hydrogen elimination,[4] which proceeds well only with bulky substituents, e.g., in the preparation of $(Me_3CCH_2)_3M{\equiv}CCMe_3$ (M = Mo, W).[2,5] The central compounds for this chemistry, however, are the trichloro complexes, e.g., dimethoxyethane (DME)-stabilized $Cl_3(DME)M{\equiv}CCMe_3$ (M = Mo, W), which are obtained from the trisneopentyl(neopentylidyne)metal complexes by treatment with HCl.[2,5] Essentially all other neopentylidyne complexes can be prepared from these compounds. Analogous complexes containing other alkylidyne ligands apparently are not generally accessible, except the trisalkoxy derivatives which can be prepared by acetylene metathesis.[1,2,6]

On the other hand, the chemistry of the related metal carbyne complexes $X(CO)_4M{\equiv}CR$ (X = halide, M = Cr, Mo, W; *R* = alkyl, aryl), developed by Fischer and his group,[7] is much less restricted in the choice of the carbyne, or alkylidyne, ligands. However, no methods are known for the oxidative conversion of monohalotetracarbonylmetal carbyne complexes into trihalometal carbyne complexes.[8] Availability of such procedures would considerably facilitate exploration of the chemistry of metal-carbon triple bonds. We wish to report a simple procedure for bromine oxidation of *trans*-$Br(CO)_4M{\equiv}CR$ (M = Mo, W; R = alkyl, aryl). It provides an efficient general synthesis of tribromometal alkylidyne complexes of molybdenum and tungsten in combination with previously developed routes to metal carbyne complexes based on oxide abstraction from acyl ligands[9] and double β-addition of electrophiles to acetylide ligands.[10]

The key step of the successful oxidation is the low-temperature reaction of the *trans*-bromotetracarbonylmetal carbyne complexes, $Br(CO)_4M{\equiv}CR$, **1-4**, with an equivalent amount of bromine in dichloromethane solution. The initial low-temperature intermediates decompose upon warming under loss of carbon monoxide and in the presence of dimethoxyethane the DME stabilized tribromometal alkylidyne complexes $Br_3(DME)M{\equiv}CR$, **5-8**, form. The reactions proceed well for molybdenum and tungsten systems but not for the chromium analogues.[8] Aliphatic as well as aromatic carbyne ligands are suitable.

$Br(CO)_4M{\equiv}CR$
1, M = Mo, R = C_6H_5
2, M = W, R = C_6H_5
3, M = W, R = CH_3
4, M = W, R = $CH_2C(CH_3)_3$

$$\xrightarrow[\substack{CH_2Cl_2\\ -95 \text{ or } -78\ ^\circ C \rightarrow \text{room temperature}}]{Br_2,\ DME} \begin{matrix} Br_3(DME)M{\equiv}CR \\ \textbf{5},\ M = Mo,\ R = C_6H_5 \\ \textbf{6},\ M = W,\ R = C_6H_5 \\ \textbf{7},\ M = W,\ R = CH_3 \\ \textbf{8},\ M = W,\ R = CH_2C(CH_3)_3 \end{matrix} \quad (1)$$

The carbyne complexes **1**, **2**, and **3** are generated by reaction of the corresponding pentacarbonylmetal acyl complexes $NMe_4[(CO)_5M{-}C(O)R]$ **9**, **10**, and **11** (**9**, M = Mo, R = C_6H_5; **10**, M = W, R = C_6H_5; **11**, M = W, R = CH_3) with oxalyl bromide in methylene chloride at low temperatures (**9**, -78 °C; **10**, -78 to -20 °C; **11**, -95 to -20 °C).[9] Formed NMe_4Br is removed by filtration at -78 °C. The initial solutions of the phenylcarbyne complexes **1** and **2** are of sufficient high purity for the direct further reaction with bromine. In succession, a tenfold excess of DME and a cold CH_2Cl_2 solution (-78 °C) of an equivalent amount of bromine are added. The red reaction solutions of **1** and **2** are allowed to warm up slowly to room temperature. Recrystallization[18] of the products from CH_2Cl_2/pentane affords **5**[11] as brown microcrystals and **6**[12] as dark green crystals in 80% and 90% yield, respectively. Thus, the tribromometal benzylidyne complexes of molybdenum and tungsten are prepared in a single procedure from the easily available pentacarbonylmetal acyl complexes (eq 2).

$$NMe_4[(CO)_5M{-}C(O)Ph] \xrightarrow[\substack{2.\ DME,Br_2,\\ CH_2Cl_2}]{1.\ C_2O_2Br_2} Br_3(DME)M{\equiv}CPh \quad (2)$$

M = Mo, W

Analogous direct oxidation of the methylcarbyne complex **3** has not proved to be successful reproducibly. Apparently, already small amounts of impurity in the initial carbyne complex solution—presumably due to decomposition of rather labile **3** or minor side products in the reaction of **11** with oxalyl bromide—adversely affect the reaction with bromine. Thus, compound **3** is purified by chromatographic methods.[13] Similarly, the carbyne complex $Br(CO)_4W{\equiv}CCH_2CMe_3$ (**4**)—obtained by double protonation of $NEt_4[(CO)_5W{-}C{\equiv}CCMe_3]$ with CF_3SO_3H and addition of NEt_4Br[10]—is first isolated in pure form.[14] Bromine

(1) (a) Wengrovius, J. H.; Sancho, J.; Schrock, R. R. *J. Am. Chem. Soc.* **1981**, *103*, 3932-3934. (b) Churchill, M. R.; Ziller, J. W.; Freudenberger, J. H.; Schrock, R. R. *Organometallics* **1984**, *3*, 1554-1562. (c) Freudenberger, J. H.; Schrock, R. R.; Churchill, M. R.; Rheingold, A. L.; Ziller, J. W. *Organometallics* **1984**, *3*, 1563-1573.

(2) (a) McCullough, L. G.; Schrock, R. R. *J. Am. Chem. Soc.* **1984**, *106*, 4067-4068. (b) McCullough, L. G.; Schrock, R. R.; Dewan, J. C.; Murdzeck, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 5987-5998.

(3) (a) Pedersen, S. F.; Schrock, R. R.; Churchill, M. R.; Wassermann, H. J. *J. Am. Chem. Soc.* **1982**, *104*, 6808-6809. (b) Schrock, R. R.; Pedersen, S. F.; Churchill, M. R.; Ziller, J. W. *Organometallics* **1984**, *3*, 1574-1583.

(4) Schrock, R. R. *Acc. Chem. Res.* **1979**, *12*, 98-104.

(5) (a) Clark, D. N.; Schrock, R. R. *J. Am. Chem. Soc.* **1978**, *100*, 6774-6776. (b) Schrock, R. R.; Clark, D. N.; Sancho, J.; Wengrovius, J. H.; Rocklage, S. M.; Pedersen, S. F. *Organometallics* **1982**, *1*, 1645-1651.

(6) (a) Schrock, R. R.; Listemann, M. L.; Sturgeoff, L. G. *J. Am. Chem. Soc.* **1982**, *104*, 4291-4293. (b) Listemann, M. L.; Schrock, R. R. *Organometallics* **1985**, *4*, 74-83. (c) Strutz, H.; Schrock, R. R. *Organometallics* **1984**, *3*, 1600-1601.

(7) Fischer, E. O.; Schubert, U. *J. Organomet. Chem.* **1975**, *100*, 59-81.

(8) Oxidation reactions of $Br(CO)_4CrCPh$ with strong oxidizing agents such as Cl_2 or Br_2 have been reported. Only complete degradation of the complex was observed. Fischer, E. O.; Ruhs, A.; Kalder, H. J. *Z. Naturforsch., B* **1977**, *32B*, 473-475.

(9) Mayr, A.; McDermott, G. A.; Dorries, A. M. *Organometallics* **1985**, *3*, 608-610.

(10) Mayr, A.; Schaefer, K. C.; Huang, E. Y. *J. Am. Chem. Soc.* **1984**, *106*, 1517-1518.

(11) **5**: Anal. Calcd for $C_{11}H_{15}Br_3O_2Mo$: C, 25.66; H, 2.94; Br, 46.56. Found: C, 25.50; H, 3.03; Br, 46.87. ^{13}C NMR (CD_2Cl_2, -20 °C) δ 329.2 (CPh).

(12) **6**: Anal. Calcd for $C_{11}H_{15}Br_3O_2W$: C, 21.92; H, 2.51; Br, 39.77. Found: C, 21.72; H, 2.51; Br, 39.75. ^1H NMR ($CDCl_3$) δ 7.62, 6.89, 6.69 (m, 5, C_6H_5), 4.28, (s, 3, $CH_3OCH_2CH_2OCH_3$), 4.13 (m, 2, $CH_3OCH_2CH_2OCH_3$), 4.04 (m, 2, $CH_3OCH_2OCH_2OCH_3$), 3.99 (s, 3, $CH_3OCH_2CH_2OCH_3$), ^{13}C NMR (C_6D_6) δ 331.7 (J_{CW} = 219 Hz), 138.6, 132.6, 126.5 (C_6H_5), 79.6 76.2 70.7, 61.2 ($CH_3OCH_2CH_2OCH_3$).

(13) Fischer, E. O.; Kreis, G. *Chem. Ber.* **1976**, *109*, 1673-1683.

0002-7863/86/1508-0548$01.50/0