

Experimental Section

3: Methyl triflate (**2**, 5 g, 30.5 mmol) was added to a saturated solution of **1** (485 mg, 0.88 mmol) in CH_2Cl_2 . Evaporation of solvent and excess **2** led to a yellow residue, which was dissolved in CH_2Cl_2 . After addition of hexane, **3** precipitated as an analytically pure, microcrystalline powder, which was isolated by filtration and dried under vacuum (442 mg, 0.62 mmol, yield: 70%). Crystals suitable for an X-ray structure analysis could be obtained by layering a saturated solution of **3** in CH_2Cl_2 with diethyl ether. After 5 min sufficiently large platelets appeared, which had to be removed at once from the mother liquor to avoid decomposition. M.p. 118 °C (decomp.); UV/Vis: $\lambda = 249.4$ ($\pi \rightarrow \pi^*$, P=P), 283.7 ($\pi \rightarrow \pi^*$, aryl), 364.2 ($n \rightarrow \pi^*$, P=P); ^{31}P NMR (CD_2Cl_2): $\delta = 237.0$ (d, ArCH_3P), 332.2 (d, $^1J_{\text{PP}} = 633$ Hz, ArP); ^1H NMR (CD_2Cl_2): $\delta = 1.38$ (s, 9H, *p*-*t*Bu), 1.40 (s, 9H, *p*-*t*Bu), 1.55 (d, $^5J_{\text{PH}} = 2.44$ Hz, 18H, *o*-*t*Bu), 1.60 (s, 18H, *o*-*t*Bu), 1.86 (dd, $^3J_{\text{PH}} = 19.80$, $^5J_{\text{PH}} = 4.87$ Hz, 3H, CH_3), 7.66 (dd, $^4J_{\text{PH}} = 1.83$, $^5J_{\text{PH}} = 1.83$ Hz, 2H, aryl-H), 7.70 (d, $^4J_{\text{PH}} = 5.18$ Hz, 2H, aryl-H).

Received: June 7, 1999 [Z13523IE]

German version: *Angew. Chem.* **1999**, *111*, 3546–3548

Keywords: cations • dissociation energies • multiple bonds • nitrogen • phosphorus

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- [9] Crystal data for **3**: monoclinic, space group $P2_1/m$; $a = 11.5412(2)$, $b = 14.5829(3)$, $c = 12.6593(1)$ Å, $\beta = 107.69(1)^\circ$; $V = 2029.84(6)$ Å³; $Z = 2$, $\text{Mo}_{\text{K}\alpha}$ radiation, $2\theta_{\text{max}} = 41.6^\circ$. Of 8822 reflections, 2248 were independent ($R_{\text{int}} = 0.0919$); $R_1 = 0.0654$, $wR_2 = 0.1855$ (based on F^2) for 259 parameters and 1539 reflections with $I > 2\sigma(I)$. The poorly diffracting platelet was partially merohedrally twinned (twin law: $-1\ 0\ 0\ 0 - 1\ 0\ 0\ 0\ 1$, relationship of twin components: 0.7194:0.2806). Nevertheless the structure could be solved by direct methods and was refined against full matrix (versus F^2) with SHELXTL (Version 5.0), assigning the reflections listed in the *hkl* file to each twin component. Owing to the poor data-to-parameter ratio non-hydrogen atoms were refined with restricted anisotropic displacement parameters using SIMU and ISOR instructions. One *p*-*t*Bu group was refined isotropically as a rigid group disordered over two positions with relative occupancy factors of 0.8 and 0.2. Hydrogen atoms were refined on calculated positions using the riding model or as rigid groups. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-120592. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

- [10] **6:** At room temperature, only an exchanged-broadened ^{31}P NMR signal is observed; the *meso* form **6** is the dominant diastereomer at low temperatures. M.p. 186 °C; ^{31}P NMR (CDCl_3 , -60°C): **6**: $\delta = -32.4$ (s); **6'**: $\delta = -35.8$ (s). The *meso* isomer **6** was also characterized by X-ray structure analysis, and showed no special features (P=P: 2.216(1) Å; $\Sigma^\circ(\text{P}) = 315.9$: monoclinic, space group $P2_1/c$; $a = 11.0304(4)$, $b = 19.3032(10)$, $c = 18.2587(8)$ Å, $\beta = 102.003(2)^\circ$; $V = 3802.7(3)$ Å³; $Z = 4$. Further details can be obtained from the authors.
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Polyoxometalates as Reduction Catalysts: Deoxygenation and Hydrogenation of Carbonyl Compounds**

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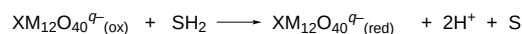
Investigations concerning the use of polyoxometalates as catalysts in both liquid and gas-phase reactions have intensified significantly over the last decade. These catalytic applications in acid catalysis^[1] and oxidation^[2] have taken advantage of the strong Brønsted acidity of heteropoly acids and the inherent stability of the polyoxometalate framework to oxidative degradation in the presence of strong oxidants and at high temperatures. Although a few examples of

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[**] The Israel Electric Company is thanked for their generous support in funding a fellowship for V.K.

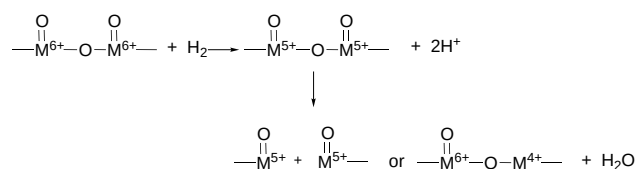
reductions catalyzed by noble metals (Pt, Pd, Rh, and Ir) in the presence of polyoxometalates have been reported,^[3] the use of polyoxometalates alone as reduction catalysts has yet to be disclosed.

The redox activity of polyoxometalates, especially of the Keggin type, has often been utilized, whereby the polyoxometalate in the oxidized form oxidizes a substrate (SH₂) that by definition is a reducing agent (Scheme 1). The reduced



Scheme 1. Oxidation of a substrate SH₂ with a polyoxometalate as well as reduction of the polyoxometalate. X = P, Si; M = W, Mo, V.

form is subsequently reoxidized, commonly by oxygen, to complete the catalytic cycle. Importantly, in this reaction mode the substrate may also be hydrogen.^[4] Thus, at 250–300 °C reduction of polyoxometalates by hydrogen (Scheme 2) has been reported.



Scheme 2. Reduction of a polyoxometalate—represented schematically by M(O)–O–M(O)—with hydrogen.

Here we report on the activation of hydrogen by Keggin-type polyoxometalates and the utilization of the reduced polyoxometalate species for the catalytic deoxygenation of ketones and aldehydes, a reaction classically carried out by the Clemmensen and Wolff–Kishner reactions. The products formed from the polyoxometalate-catalyzed deoxygenation depend strongly on the type of polyoxometalate used (tungstate or vanadomolybdate). The reaction does not appear to involve a carbinol intermediate, and the polyoxometalate was shown to be structurally stable under the reaction conditions.

The polyoxometalate catalysts (as potassium salts) were used supported on γ -alumina (surface area $\approx 200 \text{ m}^2 \text{ g}^{-1}$); reactions were run without solvent in a 300-mL Parr autoclave at 300 °C. γ -Alumina and potassium heteropoly salts (pH 6 in aqueous solution), prepared by cation exchange from the original heteropoly acids, were used to reduce acidity and thus minimize cracking and other acid-catalyzed reactions. In the first stage, the catalytic activity of various polyoxometalates was compared using benzophenone as substrate (Table 1). Two trends were observed. The order of catalytic activity was $[\text{SiW}_{12}\text{O}_{40}]^{4-} < [\text{PW}_{12}\text{O}_{40}]^{3-} < [\text{PMo}_{12}\text{O}_{40}]^{3-} < [\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^{5-}$, which correlates with the reducibility with H₂ and the oxidation potentials of the polyoxometalates.^[5] For $[\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^{5-}$ the conversion into diphenylmethane was quantitative. In other words, the more facile the activation of H₂ as outlined in Scheme 2, the higher the conversion. For transition metal substituted polyoxometalates $[\text{SiM}(\text{H}_2\text{O})\text{W}_{11}\text{O}_{39}]^{q-}$, the most stable series, a positive affect

Table 1. Reduction of benzophenone by various polyoxometalates.^[a]

Catalyst	Conversion [mol %]
K ₄ SiW ₁₂ O ₄₀ /Al ₂ O ₃	41
K ₆ SiCo(H ₂ O)W ₁₁ O ₃₉ /Al ₂ O ₃	48
K ₆ SiCu(H ₂ O)W ₁₁ O ₃₉ /Al ₂ O ₃	83 ^[b]
K ₆ SiNi(H ₂ O)W ₁₁ O ₃₉ /Al ₂ O ₃	34
K ₅ SiCr(H ₂ O)W ₁₁ O ₃₉ /Al ₂ O ₃	46
K ₃ PW ₁₂ O ₄₀ /Al ₂ O ₃	70
K ₃ PMo ₁₂ O ₄₀ /Al ₂ O ₃	95
K ₅ PV ₂ Mo ₁₀ O ₄₀ /Al ₂ O ₃	100

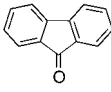
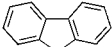
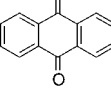
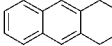
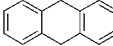
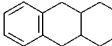
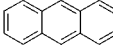
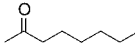
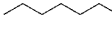
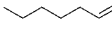
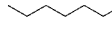
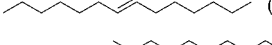
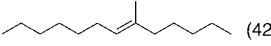
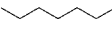
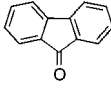
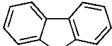
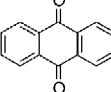
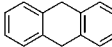
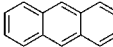
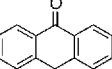
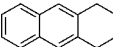
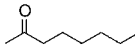
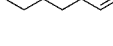
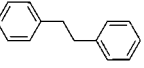
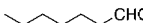
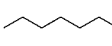
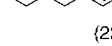
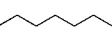
[a] Reaction conditions: 0.5 g (2.75 mmol) of benzophenone, 1 g of catalyst (50 mg (16–20 μmol) of polyoxometalate), 23 atm H₂, $T = 300^\circ\text{C}$, $t = 200$ min. Unless stated otherwise, the sole product was diphenylmethane. [b] 1,1,2,2-Tetraphenylethane was a by-product (6–7 %).

was observed for substitution with Cu^{II}, while Co^{II}, Cr^{III}, and Ni^{II} had no significant influence.

After observing the high activity in benzophenone deoxygenation, we investigated the reductive deoxygenation of various other benzylic, cyclic, and acyclic ketones and aldehydes (Table 2). The differences between supported $[\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^{5-}$ and $[\text{SiW}_{12}\text{O}_{40}]^{4-}$ as catalysts are striking. As in the case of benzophenone, K₅PV₂Mo₁₀O₄₀/Al₂O₃ was significantly more active than K₄SiW₁₂O₄₀/Al₂O₃. For simple benzylic ketones such as benzophenone, fluorenone, and acetophenone, the sole products for both $[\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^{5-}$ and $[\text{SiW}_{12}\text{O}_{40}]^{4-}$ were the simple methylene derivatives, formally formed by deoxygenation and addition of hydrogen. However, other substrates, especially aliphatic ketones and aldehydes, provided very different product selectivities. For 9,10-anthraquinone, use of $[\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^{5-}$ leads to formation of mostly the more highly reduced species, tetra- and octahydroanthracene, along with dihydroanthracene and anthracene but no anthrone, while $[\text{SiW}_{12}\text{O}_{40}]^{4-}$ yielded for the most part less highly reduced products. In the case of cycloheptanone and 2-octanone, it was observed again that $[\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^{5-}$ catalyzed formation of mostly saturated compounds (cycloheptane/ethylcyclopentane and octane, respectively). In contrast, upon use of $[\text{SiW}_{12}\text{O}_{40}]^{4-}$ only alkenes (cycloheptene/methycyclohexene and octenes) and a rearranged alkene (norbornane) were detected. These alkenes were not significantly reduced even after extended reaction periods of 48 h. In the case of benzaldehyde, toluene was the major product for both catalysts, although the formation of a small amount of dibenzyl in the presence of $[\text{SiW}_{12}\text{O}_{40}]^{4-}$ is mechanistically significant. The most unusual reactivity was viewed upon use of an aliphatic aldehyde, *n*-heptanal, as substrate. $[\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^{5-}$ catalyzed a deoxygenation–coupling reaction to yield a mixture of tetradecene isomers and the saturated *n*-tetradecane; no C₇ products were observed. On the other hand, use of $[\text{SiW}_{12}\text{O}_{40}]^{4-}$ yielded mostly formation of the aldol condensation product (presumably due to the acidity of γ -alumina) and some tetradecene isomers, but again no C₇ products or saturated tetradecane.

It is worthwhile to present a preliminary working hypothesis concerning the reaction mechanism. As reported^[4] and shown in Scheme 2, reduction of a Keggin-type polyoxometalate with H₂ at 250–300 °C yields a deoxygenated polyoxometalate that probably contains M^{IV}. Such reduced species are effective even at room temperature for oxygen atom transfer

Table 2. Reduction of ketones and aldehydes catalyzed by $K_3PV_2Mo_{10}O_{40}$ and $K_4SiW_{12}O_{40}$.^[a]

Substrate	Conversion	Conditions	Products ^[b]
$K_3PV_2Mo_{10}O_{40}/Al_2O_3$			
	100	3.5 h, 34 atm	 (100)
	100	3.5 h, 23 atm	 (100)
	100	3.5 h, 34 atm	 (54)  (25)  (16)  (5)
	100	3.5 h, 54 atm	 (48)  (15)  (18)  (5)  (4)  (10)
	96	20 h, 54 atm	 (82) E + Z  (15)  (3)
	62	3.5 h, 23 atm	 (100)
	85	3.5 h, 23 atm	E + Z  (44)  (42)  (14)
$K_4SiW_{12}O_{40}/Al_2O_3$			
	21	3.5 h, 500 psi	 (100)
	80	3.5 h, 23 atm	 (100)
	96	3.5 h, 34 atm	 (66)  (10)  (10)  (14)
	48	3.5 h, 54 atm	 (71)  (19)  (10)
	74	20 h, 54 atm	E + Z  (100)
	85	3.5 h, 23 atm	 (96)  (4)
	69	3.5 h, 23 atm	 (60) $C_5H_{11}CHO$ E + Z  (22)  (18)

[a] Reaction conditions: 2.75 mmol of substrate, 1 g of catalyst (50 mg (16–20 μ mol) of polyoxometalate), $T = 300^\circ C$, H_2 pressure and time are give in the Table. [b] The amount of product as a percentage of the total product is given in parentheses.

from an organic substrate (such as a sulfoxide) to a M^{IV} polyoxometalate.^[6] A similar deoxygenation of a carbonyl compound can thus be contemplated. A simple experiment to test whether such a deoxygenation pathway is operative as opposed to the common hydrogenation mechanism via carbinol intermediates as observed in “hydride chemistry”^[7] was carried out using 1-heptanol as substrate. With $[PV_2Mo_{10}O_{40}]^{5-}$ at 24 atm H_2 and $300^\circ C$ mostly diheptyl ether and a little 1-heptene but no coupled products (i.e., tetradecenes) were formed. In the case of benzylic carbonyl compounds, formal addition of two hydrogen atoms after deoxygenation leads to the reduced product. For aliphatic ketones, a fast hydrogen shift after deoxygenation will lead to an alkene as initial product. In the

case of $[SiW_{12}O_{40}]^{4-}$ as catalyst, this alkene is not reduced although rearrangement reactions (thermal and/or catalytic) lead to the observed product mixture. For $[PV_2Mo_{10}O_{40}]^{5-}$, there are two possibilities to explain the formation of hydrogenated products: 1) The initial alkene formed is hydrogenated in a separate reaction or 2) addition of hydrogen occurs before the hydrogen shift. The reactivity observed for aldehyde deoxygenation also supports our working hypothesis. After deoxygenation, coupling reactions instead of hydrogen shifts are dominant for 1-heptanal but were also observed for benzaldehyde. The mechanism of this coupling is not clear, but the approximately 1:1 product ratio for 7-tetradecene:6-methyl-6-tridecene is conspicuous.

The integrity of the Keggin polyoxometalates $K_4SiW_{12}O_{40}$ and $K_5PV_2Mo_{10}O_{40}$ under the reaction conditions was also proven by IR spectroscopy and X-ray diffraction studies. A finely powdered sample of the polyoxometalate was treated under the reaction conditions (0.5 g of benzophenone, 50 mg of polyoxometalate, 23 atm H_2 , $T = 300^\circ C$, $t = 200$ min). After cooling, the autoclave was opened and the polyoxometalate was isolated by filtration. The catalyst first appeared brown-blue, but after exposure to air the color turned lighter. The IR spectra and X-ray powder patterns before and after the reaction were identical, indicating that the structure of the polyoxometalates was unchanged. A room-temperature ESR spectrum of the $PV_2Mo_{10}O_{40}^{5-}$ catalyst after reaction showed the typical eight-line spectrum of the two-electron-reduced compound.^[8] That no leaching of the polyoxometalate from the support occurred was indicated by atomic absorption measurements of the organic phase after extraction with water.

We have demonstrated a new application of Keggin polyoxometalates as deoxygenation and hydrogenation catalysts for the reduction of carbonyl compounds. The $[PV_2Mo_{10}O_{40}]^{5-}$ polyoxometalate, which is most active for the activation (oxidation) of H_2 , is the most active catalyst. The product selectivity shows that the reduced polyoxometalates deoxygenate ketones and aldehydes; carbinols are not intermediates. Use of $[PV_2Mo_{10}O_{40}]^{5-}$ tends to lead to formation of saturated compounds, whereas for $[SiW_{12}O_{40}]^{4-}$ alkenes are preferred initial products.

Experimental Section

Solutions of $H_3PW_{12}O_{40}$, $H_3PMo_{12}O_{40}$, $H_4SiW_{12}O_{40}$, and $H_5PV_2Mo_{10}O_{40}$ ^[9] were treated on an Amberlyst 120 (K^+ form) ion-exchange column to prepare the polyoxometalates $K_3PW_{12}O_{40}$, $K_3PMo_{12}O_{40}$, $K_4SiW_{12}O_{40}$, and $K_5PV_2Mo_{10}O_{40}$. $K_6SiM(H_2O)W_{11}O_{39}$ ($M = Co^{II}$, Cu^{II} , Ni^{II}) and $K_5SiCr^{III}(H_2O)W_{11}O_{39}$ were prepared by the literature procedure.^[10] The polyoxometalates were wet impregnated from water on γ -alumina at a 5 wt % loading and dried at $100^\circ C$ overnight. Reactions were run in a stirred Parr autoclave at $300^\circ C$ and 23–54 atm H_2 . Specific conditions are given in the Table legends. The reaction products were analyzed by GC and GC-MS using an apolar methylsilicone column.

Received: February 19, 1999

Revised version: June 24, 1999 [Z13061IE]

German version: *Angew. Chem.* **1999**, *111*, 3551–3554

Keywords: deoxygenations • heterogeneous catalysis • hydrogenations • polyoxometalates • reductions

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Total Synthesis of Everninomicin 13,384-1— Part 1: Synthesis of the $A_1B(A)C$ Fragment**

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*Dedicated to Dr. A. K. Ganguly
on the occasion of his 65th birthday*

Drug-resistant bacteria are currently causing considerable concern because of the serious and constant threat they pose to human health and their potential to cause widespread epidemics. Even vancomycin,^[1] whose effectiveness against such resistant bacterial strains provided the last line of defense, is showing signs of weakness in the face of the evolution of aggressive bacteria. Everninomicin 13,384-1 (Ziracin) (**1**),^[2] a member of the orthosomicin class of antibiotics^[3] and currently in clinical trials, is a promising new weapon against drug-resistant bacteria, including methicillin-resistant staphylococci and vancomycin-resistant streptococci and enterococci.^[4] Isolated from *Micromonospora carbonacea* var. *africana* (found in a soil sample collected from the banks of the Nyiro River in Kenya), everninomicin 13,384-1 (**1**) possesses a novel oligosaccharide structure containing two sensitive orthoester moieties and terminating with two highly substituted aromatic esters. In addition, **1** contains a 1→1'-disaccharide bridge, a nitrosugar (everni-

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[**] We thank Dr. A. K. Ganguly for helpful discussions and a generous gift of everninomicin 13,384-1 and Drs. D. H. Huang, G. Siuzdak, and R. Chadha for NMR spectroscopic, mass spectroscopic, and X-ray crystallographic assistance, respectively. This work was financially supported by the National Institutes of Health (USA), The Skaggs Institute for Chemical Biology, postdoctoral fellowships from M.E.C., Spain (R.M.R.; Fulbright), the Japan Society for the Promotion of Science (H.S.), the George Hewitt Foundation (K.C.F.), and Ligue Nationale contre le Cancer (O.B.), and grants from Schering Plough, Pfizer, Glaxo, Merck, Hoffmann-La Roche, DuPont, and Abbott Laboratories.