Dendritic Phosphonates and the *in situ* Assembly of Polyperoxophosphotungstates: Synthesis and Catalytic Epoxidation of Alkenes with Hydrogen Peroxide

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Abstract: First and second-generation rigid dendrimers based on polyphenylated tetrahedral adamantane cores with four or sixteen peripheral phosphonate moieties, PD1 and PD2, respectively, were synthesized and characterized. Further reaction of the dendritic phosphonates with tungstic acid in the presence of hydrogen peroxide led to the stepwise *in situ* formation of mono- and dinuclear phosphoperoxotungstates. These assemblies were effective catalysts for the epoxidation of alkenes in an aqueous acetonitrile solvent.

Keywords: catalysis, dendrimer, oxidation, phosphonates, polyoxometalates

The chemistry of dendrimers is being studied for potential applications in many diverse areas including magnetic resonance imaging, drug-delivery, gene-delivery vectors, and others.[1] One intensively studied application has been in the area of catalysis where metallodendritic compounds appear as a novel generation of catalysts that have the catalytic properties of homogeneous catalysts but may be easily separated after use. This feature is essential for high reaction efficiency, and economical and environmental reasons.[2] Membrane reactors, nanofiltration and centrifugation are efficient separation techniques for this purpose. Indeed, many periphery-functionalized dendritic catalysts that can catalyze cross-coupling reactions, hydrogenation, hydroformylation, polymerization, allylic alkylation and other important transformations have been described,[2] but only relatively few dendritic catalysts for catalytic oxidation have been disclosed. Notable examples are (i) core-functionalized dendritic metalloporphyrins as biomimetic analogues of heme oxygenases for regio- and shape-selective epoxidation of alkenes and oxidation of sulfides,[3] (ii) polyorganotellurides based on Frechét-type dendrimers that catalyze the oxidation of thiophenol with hydrogen peroxide,[4] (iii) polyoxometalate terminated dendrimers based on esterificaton of the $[H_4P_2V_3W_{15}O_{62}]^{12-}$ polyoxometalate anion with dendritic polyols active for thiolane oxidation by *tert*-butyl hydroperoxide,[5] and (iv) quaternary ammonium-based dendrimers that electrostatically bind peroxophosphotungstates and activate hydrogen peroxide for alkene epoxidation.[6]

The synthesis of polyoxometalates is often carried out by mixing the stoichiometrically required amounts of monomeric metal salts.[7] Similarly, the catalytically active tetra(diperoxotungsto)phosphate, $\{(PO_4)[W_2O_2(\mu\text{-}O_2)_2(O_2)_2]_2\}^{3-}$, can be prepared directly from oxodiperoxotungstate and phosphoric acid.[8] Subsequent studies have revealed that diperoxotungten species such as $[W(O)(O_2)_2(H_2O)_2]$ can bind not only to $[PO_4]^{3-}$, but also to other assembling ions such as $[AsO_4]^{3-}$, $[HAsO_4]^{2-}$, $[HPO_4]^{2-}$, $[SO_4]^{2-}$ and their organic analogues such as $[CH_3AsO_3]^{2-}$, $[PhPO_3]^{2-}$, and others. Many of these compounds are excellent catalysts for oxidation of alkenes and alcohols with aqueous hydrogen peroxide.[9] We have now utilized the assembly of diperoxotungstate to phosphonate groups[9g] in order to prepare two generations of dendritic analogues based on a rigid structure with a tetrahedral adamantanyl core. The peroxophosphonatotungstates were assembled *in situ* yielding catalyst *mixtures* for the hydrogen peroxide-mediated epoxidation of alkenes. The assembled catalyst mixtures are water-soluble, thus allowing their easy separation from the reaction substrates and products; however, this water solubility did not compromise their catalytic activity towards hydrophobic substrates.

The synthesis of first generation dendrimer, the tetrahedral-shaped tetrakis-1,3,5,7-(4-phosphonatophenyl)-adamantane (**PD1**; Scheme 1), began by synthesis of

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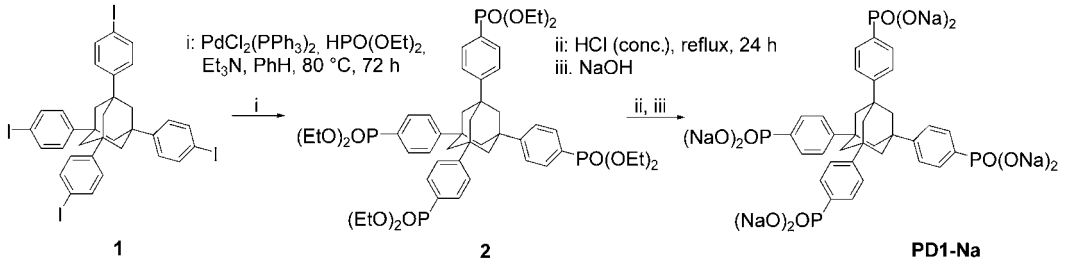
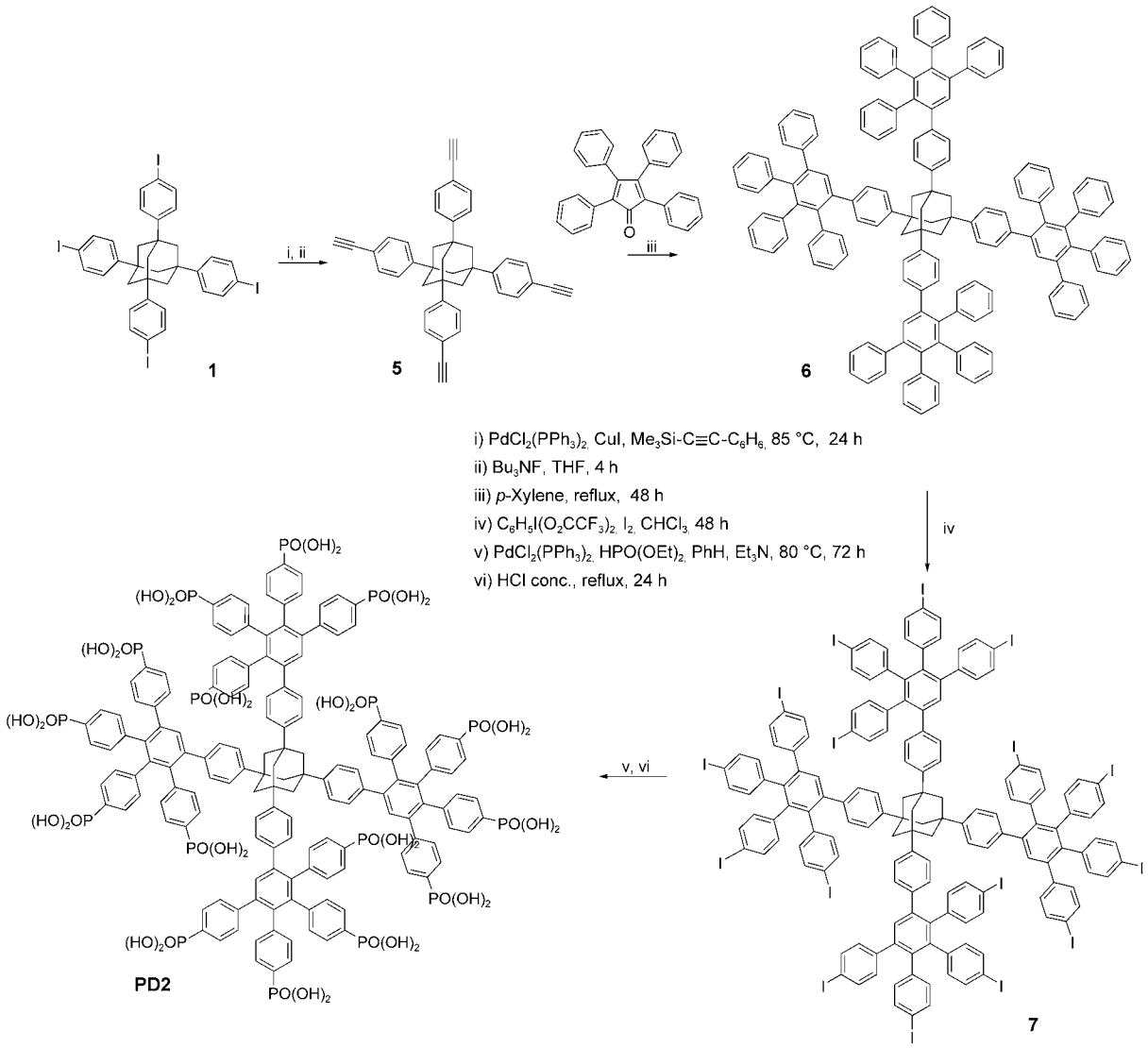


Scheme 1. Synthesis of the first generation dendrimer, sodium tetrakis-1,3,5,7-(4-phosphonatophenyl)adamantane (**PD1-Na**).



Scheme 2. The synthesis of the second generation dendrimer, hexadecaphosphonic acid **PD2**.

1,3,5,7-tetraphenyladamantane followed by iodination with iodine and [bis(trifluoroacetoxy)iodo]benzene leading to tetrakis-1,3,5,7-(4-iodophenyl)adamantane (**1**) according to a literature procedure.[10] Tetrakis-1,3,5,7-(4-diethylphosphonatophenyl)adamantane (**2**) was prepared by a palladium-catalyzed P–C coupling reaction of **1** and diethyl phosphite. Acidic hydrolysis of **2** gave **PD1**, which appeared to be poorly soluble in water. In order to increase its solubility the octasodium salt, **PD1-Na** was prepared.

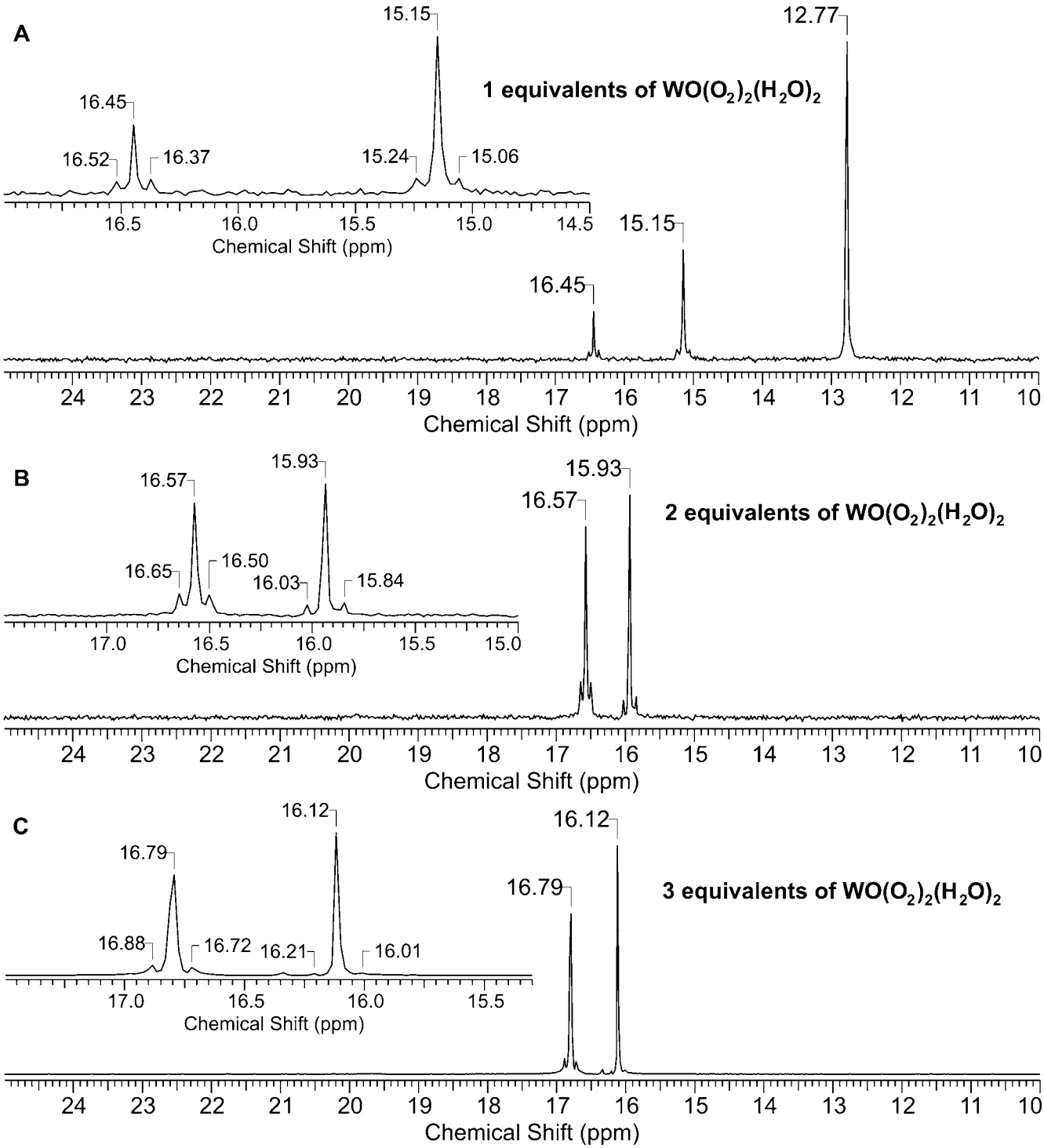


Figure 1. ^{31}P NMR spectra of 4-MePhPO(ONa)$_2$ in a $H_2O/H_2O_2/CD_3CN$ mixture in the presence of different amounts of $[W(O)(O_2)_2(H_2O)_2]$.

Synthesis of the second generation dendritic hexadecaphosphonate **PD2** (Scheme 2) began by the Pd-catalyzed Sonogashira coupling reaction of **1** with triisopropylsilylethyne to yield **4** followed by deprotection of terminal alkyne to yield tetrakis-1,3,5,7-(4-ethynylphenyl)-adamantane (**5**). The tetrahedral polyphenylene dendrimer, **6**, was prepared by a [2+4] cycloaddition-decarbonylation reaction of **5** with tetraphenylcyclopentadienone.[11] Iodination followed by a Pd-catalyzed P–C coupling reaction and acid hydrolysis yielded the hexadecaphosphonic acid **PD2**.

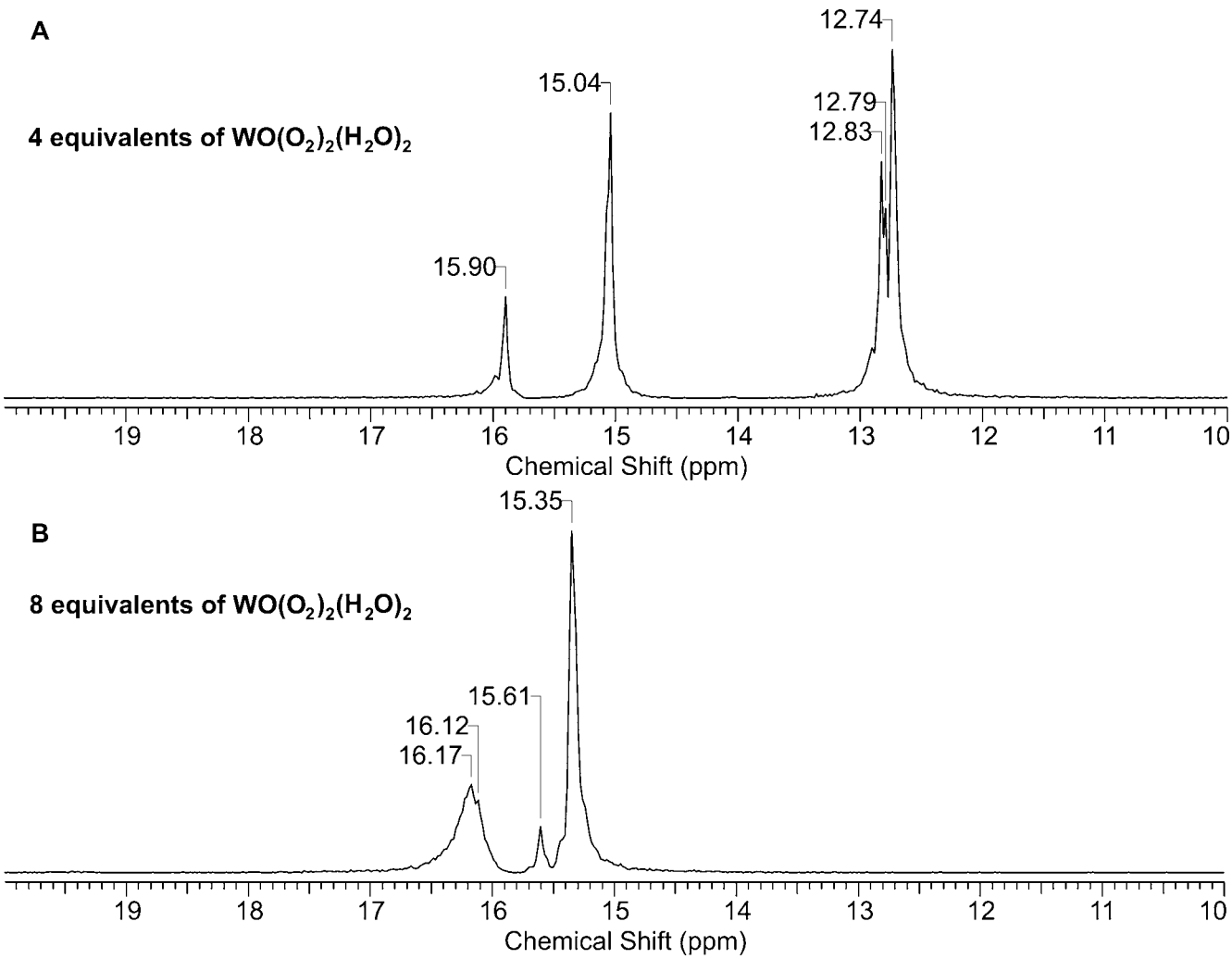


Figure 2. ^{31}P NMR spectra of **PD1-Na** in a $H_2O/H_2O_2/CD_3CN$ mixture in the presence of different amounts of $[W(O)(O_2)_2(H_2O)_2]$.

The *in situ* assembly of the peroxophosphonatotungstate catalytic species was followed by ^{31}P NMR. In Figure 1 one may observe the ^{31}P NMR spectra upon addition of one, two and three equivalents of the diperoxotungten species, $[W(O)(O_2)_2(H_2O)_2]$, to an aqueous solution of the monomeric 4-methylphenylphosphonic acid disodium salt, 4-MePhPO$(ONa)_2$.

Upon addition of one equiv. of $[W(O)(O_2)_2(H_2O)_2]$, Figure 1A, one may observe that three phosphorus-containing species are obtained, including the parent compound 4-MePhPO$(ONa)_2$ at 12.77 ppm, and two species shifted down-field appearing at 15.15 and 16.45 ppm. These are clearly phosphotungstate species as evidenced by the ^{183}W satellites ($^2J_{P,W} \approx 15$ Hz) and are formulated as the mononuclear $\{(4\text{-MePhPO}_3)[WO(O_2)_2(H_2O)]\}^{2-}$ and the dinuclear $\{(4\text{-MePhPO}_3)[WO(O_2)_2(H_2O)]_2\}^{2-}$.[9g] From the peak areas, it is also clear that the assembly of the peroxophosphonatotungstate species is not quantitative. Upon addition of two equivalents of $[W(O)(O_2)_2(H_2O)_2]$, Figure 1B, the assembly process is completed with the formation of a ~1:1 mixture of mono- and dinuclear peroxophosphonatotungstates; some $[W(O)(O_2)_2(H_2O)_2]$ remains unbound to the phosphonate. This was verified by ^{183}W NMR which showed two peaks at -621 and -689 ppm attributable to the peroxophosphotungstates and $[W(O)(O_2)_2(H_2O)_2]$, respectively. Further addition of peroxotungstate, Figure 1C, does not change the picture although very small amounts, $<1\%$, of an unidentified phosphorus containing species (16.34 ppm) were formed.

A virtually identical assembly process was observed with the dendritic phosphonate **PD1-Na**, Figure 2, although the ^{183}W satellites are more poorly resolved. Here upon addition of four equivalents of $[W(O)(O_2)_2(H_2O)_2]$, Figure 2A, various mono- and dinuclear peroxophosphonatotungstate compounds are formed, as evidenced by the peaks at 15.04 and 15.90 ppm, respectively. The cluster of peaks at ~12.7 ppm is attributable to isomeric species (non-complexed and complexed phos-

Table 1. Alkene epoxidation with aqueous H_2O_2 catalyzed by *in situ* assembled catalytic systems.

Substrate	Conversion [mol %][a]			Selectivity [mol %][b]		
	PD1-Na	$ArPO_3Na_2$	No RPO_3Na_2[c]	**PD1-Na**	$ArPO_3Na_2$	No RPO_3Na_2[c]
1-octene	68	65	37	92	94	5
E-2-octene	91	82	54	93	99	6
cyclooctene	>99	97	>99	>99	>99	66
cyclododecene	92	90	81	>99	>99	12

Reaction conditions: 1 mmol alkene, 20 μmol H_2WO_4, 5.1 μmol **PD1-Na** or 20 μmol 4-$MePhPO_3Na_2$, 0.1 mL 60% H_2O_2 (2 mmol), 0.25 mL CH_3CN, 70 °C, 5 h.
[a] Conversion is mol % alkene reacted.
[b] Selectivity is mol % epoxide formed; other products were aldehydes and acids for linear alkenes and diols, diketones and ring cleavage products for cyclic alkenes.
[c] Without phosphonate.

phonates at the arms of the dendrimer). Addition of eight equivalents of $[W(O)(O_2)_2(H_2O)_2]$ completes the assembly process, Figure 2B. Attempts to crystallize these assembled mixtures of catalytic compounds were expectedly unsuccessful, but the IR spectra of the precipitated compound shows the expected peaks at 950 cm^{-1} [ν(W=O) for the terminal oxo group], 847 cm^{-1} [ν(O–O) for the peroxo fragments], and 1100–1030 cm^{-1} [ν(P–O) for the phosphorus-oxygen stretching modes]. It is worthwhile mentioning that the incomplete complexation of peroxotungstates to the dendritic phosphonate implies a dynamic solution behavior due to continuous association-dissociation processes and the existence of various peroxophosphotungstates in equilibrium.

Catalytic epoxidation of alkenes was carried by first assembling the peroxophosphotungstate species by dissolving 20 μmol tungstic acid and 5.1 μmol **PD1-Na** in 0.1 mL H_2O_2 (aqueous 60%, 2 mmol) and 0.25 mL acetonitrile. After dissolution and assembly of the catalyst mixture the substrate (1 mmol) was added and then the reaction solution was brought to 70 °C. The results presented in Table 1 show that the catalytic mixture satisfactorily catalyzed the epoxidation of simple cyclic and linear alkenes. Moderate to excellent conversions and high selectivity to epoxide was observed. There was no significant dendrimeric effect as the use of 20 μmol 4-$MePhPO(ONa)_2$ instead of **PD1-Na** gave a similar result in the epoxidation reaction. The use of the **PD2-Na** dendrimer (20 μmol H_2WO_4, 1.2 μmol **PD2-Na**, 0.1 mL H_2O_2, 0.25 mL acetonitrile, 1 mmol *E*-2-octene, 70 °C, 5 h) for the epoxidation of 2-octene as a model substrate gave a lower conversion (62% *versus* 91% for **PD1-Na**) but higher selectivity (98% *versus* 93%).[12] Interestingly, it would appear that both the dendritic and monomeric phosphonates also are buffering agents because in their absence there was only a very low epoxide yield,[13] although moderate conversions were observed presumably due to catalysis by the acidic solution of $[W(O)(O_2)_2(H_2O)_2]$. For this reason also using a smaller amount of **PD1-Na** (1.25 μmol) gave a significantly less selective epoxidation reaction even though the amount of peroxophosphotungstate species formed *in situ* is probably similar, Figure 2.

The recycle, recovery and reuse of the catalyst mixture was quite simple and was achieved by phase separation. For example, cyclododecene (1 mmol) was oxidized in the presence of the PD1-Na based catalyst assembled as described above. The product was phase separated from the catalyst by addition of 1 mL of ethyl acetate and 0.1 mL of water. The aqueous phase was concentrated by evaporation of the water and new portions of substrate and hydrogen peroxide were added. There was no observable loss of activity over three reaction cycles: 93%, 92%, and 95% conversion, respectively at >99% selectivity to epoxide.

In conclusion, novel dendritic phosphonates have been prepared and used to assemble *in situ* peroxophosphotungstate species that are active and selective for the epoxidation of simple alkenes with hydrogen peroxide. A simple catalytic reaction protocol allows for the reuse of the catalyst mixture.

Experimental Section

Synthesis and Characterization

Details of the synthetic procedures and characterization of the compounds are given in the supporting information.

General Procedure for the Catalytic Oxidation of Alkenes by Assembled Polyphosphoperoxotungstates

Reactions were carried out in 4-mL vials, equipped with a magnetic stirring bar. In a typical reaction, the specific substrate (1 mmol) was added to a mixture of 0.25 mL of acetonitrile, tungstic acid (0.02 mmol), PD1-Na (0.0053 mmol) and hydrogen peroxide (2 mmol). The resulting mixture was heated (70 °C) and stirred at a constant rate (*ca.* 1000 rpm) for all runs. After 6 h vials were cooled down by an ice bath, then opened and 1 mL of ethyl acetate was added to the reaction

mixture. The resultant mixture was stirred for 15 min. and the organic phase of the mixture was separated and dried over Na_2SO_4. The assembled catalyst remained in the aqueous phase. Conversions of the substrate were measured by GLC using a 5% phenylmethylsilicone (30 m, 0.32 mm ID, 0.25 μm coating) column. Products were identified by GC-MS analysis.

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[12] In epoxidations of other alkenes catalyzed by **PD2-Na**, conversions were also typically lower although selectivities were very similar.

[13] Weak bases are often added to catalytic epoxidation reactions with hydrogen peroxide. For a somewhat recent example using Na_2HPO_4, see: M. C. A. van Vleit, I. W. C. E. Arends, R. A. Sheldon, *Synlett* **2001**, 248–250.

