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A New Nb_{28} Cluster Based on Tungstophosphate, $[\{Nb_4O_6(OH)_4\}\{Nb_6P_2W_{12}O_{61}\}_4]^{36-}$

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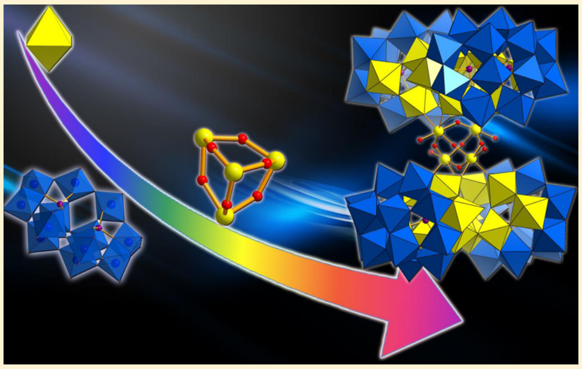
Supporting Information

ABSTRACT: A structurally intriguing polyanion, $[\{Nb_4O_6(OH)_4\}\{Nb_6P_2W_{12}O_{61}\}_4]^{36-}$ (**2**), was directly formed by controlling the reaction parameters and characterized by single-crystal X-ray diffraction, IR spectroscopy, and elemental analyses. Polyanion **2** is the first niobium-substituted Wells–Dawson-based tetramer and contains the largest Nb_{28} cluster encapsulated by four hexalacunary Wells–Dawson frameworks. The activities of compounds $Na_{12}[H_{24}$-**2**]$\cdot 24H_2O$ (**2a**), $K_{12}[H_2P_2W_{12}O_{48}]\cdot 24H_2O$, and $K_7[HNb_6O_{19}]\cdot 13H_2O$ against three human tumor cell lines were investigated in vitro. The preliminary results revealed that **2a** could efficiently inhibit the growth of the human breast cancer MCF-7 cells. Interestingly, the activity of **2a** is significantly better than those of the simple reagents.



INTRODUCTION

Transition-metal-substituted polyoxometalates (TMSPs) represent one of the most vibrant and expanding fields in polyoxometalate (POM) chemistry.[1] This is mainly due to the identification of lacunary POM species in which vacancies in the framework may be occupied by additional metal ions in order to generate a plethora of new species.[2] The metastable synthon α-$[H_2P_2W_{12}O_{48}]^{12-}$ (abbreviated as $\mathbf{P_2W_{12}}$), a hexavacant tungstophosphate derived from the plenary $[\alpha$-$P_2W_{18}O_{62}]^{6-}$ Wells–Dawson cluster by base degradation, has been utilized in the assembly of larger dimeric,[3] trimeric,[4] and tetrameric[5] aggregates. Examples are the iron-containing derivatives $\{Fe_8P_4W_{28}\}$,[3a] $\{Fe_6P_6W_{48}\}$,[4a] $\{Fe_9P_2W_{12}\}$,[5a] and $\{Fe_{27}P_8W_{49}\}$,[5a] the manganese-containing derivatives $\{Mn_6P_6W_{48}\}$,[4b] $\{Mn_2P_6W_{41}\}$,[4c] and $\{Mn_{40}P_{32}W_{224}\}$,[5b] the cobalt-containing derivatives $\{Co_2P_4W_{26}\}$,[3b] $\{Co_6P_6W_{39}\}$,[4d] and $\{Co_6P_6W_{48}\}$,[4e] the nickel-containing derivatives $\{Ni_6P_6W_{48}\}$,[4a] $\{Ni_4P_6W_{41}\}$,[4c] and $\{Ni_6P_6W_{39}\}$,[4d] the copper-containing derivative $\{Cu_4P_6W_{41}\}$,[4c] and the uranium-containing derivative $\{U_6P_6W_{36}\}$.[4f] All of these examples suggest that $\mathbf{P_2W_{12}}$ possesses high activity to bind transition metals with an outstanding range of nuclearities and diverse structural topologies.

The class of niobium-substituted POMs was pioneered by Finke and Droege.[6] Some niobium-substituted polyoxotungstates have been reported;[7−15] most of them comprise a Keggin structure,[6−11] but few Well–Dawson clusters could also be constructed.[12−15] To the best of our knowledge, the largest number of niobium ions incorporated in POMs is still 16, such as $[Nb_4O_6(Nb_3SiW_9O_{40})_4]^{20-}$,[7d] $[Nb_4O_6(Nb_3GeW_9O_{40})_4]^{20-}$,[8a] and $[Nb_4O_6(Nb_3AsW_9O_{40})_4]^{16-}$.[8b] A comprehensive literature survey of niobium-substituted polyoxotungstates is shown in Table 1.

It is worth noting that the polyanion $[(NbO_2)_6P_2W_{12}O_{56}]^{12-}$ [abbreviated as $(NbO_2)_6P_2W_{12}$ (**1**)], reported first by Hill and co-workers as early as 1997, has received little attention.[14] To date, there is only one derivative reported, in which a Nb_{12} cluster is wrapped by two $\mathbf{P_2W_{12}}$ units.[15] Inspired by the pioneering work of Finke and Droege,[6] Hill et al.,[7,14] and Liu et al.,[8] together with our particular interest in exploring the chemistry of polyoxoniobates,[9,16] we however adopt a new one-pot synthetic strategy, utilizing **1** formed in situ as a secondary building block, to investigate in detail the interaction of $\mathbf{P_2W_{12}}$ with $[Nb_6O_{19}]^{8-}$ in aqueous solution and in the presence of peroxide.

Here we present the synthesis and structure of the gigantic tetrameric Nb_{28}-containing 48-tungsto-8-phosphate $[\{Nb_4O_6(OH)_4\}\{Nb_6P_2W_{12}O_{61}\}_4]^{36-}$ (**2**), which was isolated as a sodium salt, $Na_{12}[H_{24}\{Nb_4O_6(OH)_4\}\{Nb_6P_2W_{12}O_{61}\}_4]\cdot 24H_2O$ (**2a**). Polyanion **2** represents the largest niobium/tungsten mixed-addendum POM cluster and contains more niobium atoms than any other heteropolytungstate. Further, preliminary antitumor studies indicated that compound **2a** exhibits good activity against human breast cancer MCF-7 cells.

EXPERIMENTAL SECTION

General Methods and Materials. All reagents were used as purchased without further purification. $K_7[HNb_6O_{19}]\cdot 13H_2O$ ($\mathbf{Nb_6O_{19}}$) and $K_{12}[H_2P_2W_{12}O_{48}]\cdot 24H_2O$ ($\mathbf{P_2W_{12}}$) were synthesized

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Table 1. Survey of Known Niobium-Substituted Polyoxotungstates

polyanion	Nb_n[a]	ref
	Keggin-Based	
$[(NbO_2)SiW_{11}O_{39}]^{5-}$	1	Hill et al. (1994)[10]
$[NbPW_{11}O_{40}]^{7-}$	1	Radkov and Beer (1995)[11]
$[Nb_2K(H_2O)_4(SiW_9O_{34})_2]^{9-}$	2	Niu et al. (2012)[9]
$[(NbO_2)_3PW_9O_{37}]^{6-}$	3	Hill et al. (1998)[7e]
$[(NbO_2)_3SiW_9O_{37}]^{7-}$	3	Hill et al. (2003)[7b]
$[SiW_9Nb_3O_{40}]^{7-}$	3	Finke and Droege (1984)[6]
$[GeW_9(NbO_2)_3O_{37}]^{7-}$	3	Liu et al. (2010)[8a]
$[GeW_9Nb_3O_{40}]^{7-}$	3	Liu et al. (2010)[8a]
$[AsW_9(NbO_2)_3O_{37}]^{6-}$	3	Liu et al. (2011)[8b]
$[AsW_9Nb_3O_{40}]^{6-}$	3	Liu et al. (2011)[8b]
$[Si_2W_{18}Nb_6O_{77}]^{8-}$	6	Finke and Droege (1984);[6] Hill et al. (1999)[7c]
$[Si_2W_{18}Nb_6O_{78}]^{10-}$	6	Hill et al. (2003)[7a]
$[Ge_2W_{18}Nb_8O_{88}]^{20-}$	8	Liu et al. (2010)[8a]
$[Nb_4O_6(Nb_3SiW_9O_{40})_4]^{20-}$	16	Hill et al. (1998)[7d]
$[Nb_4O_6(Nb_3GeW_9O_{40})_4]^{20-}$	16	Liu et al. (2010)[8a]
$[Nb_4O\ _6(Nb_3AsW_9O_{40})_4]^{16-}$	16	Liu et al. (2011)[8b]
	Wells−Dawson-Based	
$[(NbO_2)P_2W_{17}O_{61}]^{7-}$	1	Hill et al. (2001)[12]
$[P_2W_{15}Nb_3O_{62}]^{9-}$	3	Finke et al. (1988)[13a]/(1990)[13b]/(1996)[13c]/(2014)[13d]
$[(NbO_2)_6P_2W_{12}O_{56}]^{12-}$	6	Hill et al. (1997)[14]
$[\{P_2W_{12}Nb_4O_{59}(NbO_2)_2\}_2]^{20-}$	12	Yue et al. (2014)[15]

[a] The number of niobium ions encapsulated by the polyanion structure.

according to the published procedure.[17] The purity of compound **2a** was confirmed by IR spectroscopy.

Synthesis of $Na_{12}[H_{24}\{Nb_4O_6(OH)_4\}\{Nb_6P_2W_{12}O_{61}\}_4]\cdot 24H_2O$ (2a). $\mathbf{Nb_6O_{19}}$ (0.30 g, 0.21 mmol) was dissolved in a solution consisting of 2.5 mL of 30% aqueous H_2O_2 and 30 mL of water with moderate stirring, resulting in a pale-yellow solution. Next, 1 M HCl_{aq} (2.5 mL, 2.5 mmol) was added dropwise to give a bright-yellow effervescent solution. (***Caution!*** *If at this stage the reaction solution became cloudy, due to a suspension of* Nb_2O_5*, the solution was discarded.*) Immediately after the addition of HCl_{aq} and while the mixture was rapidly stirred, finely powdered $K_{12}[H_2P_2W_{12}O_{48}]\cdot 24H_2O$ (0.87 g, 0.22 mmol) was added in a single step, resulting in a yellow solution. The pH of the solution was adjusted to 1.7 by a HCl solution (0.5 M), followed by stirring at 80 °C unitl the yellow color disappeared. Then, NaCl (0.36 g, 6.22 mmol) was added to the filtrate (pH ~2.8). Pale-yellow block-shaped crystals formed over a 1-month period (yield based on niobium: 0.11 g, 14%). IR (cm^{-1}): 1091(s), 1067(w), 1010(w), 956(m), 907(m), 773(s), 685(m), 590(w). Elem anal. Calcd for **2a** (M_w 16473.8 g mol^{-1}): Na, 1.7; P, 1.5; Nb, 15.8; W, 53.6. Found: Na, 1.8; P, 1.5; Nb, 16.1; W, 53.9.

IR and Elemental Analysis. IR spectra were recorded on an Avatar 360 Fourier transform infrared (FTIR) spectrophotometer using KBr pellets in the range of 4000−400 cm^{-1}. The following abbreviations were used to assign the peak intensities: s, strong; m, medium; w, weak. Niobium and tungsten elemental analyses were obtained with a PerkinElmer Optima 2100 DV inductively coupled plasma optical emission spectrometer.

X-ray Crystallography. A suitable single crystal was selected and placed in a thin glass tube via efflorescence. X-ray diffraction intensity data were recorded at 296(2) K on a Bruker Apex-II CCD diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). Structure solution and refinement were carried out with the *SHELXS-97* and *SHELXL-97* program packages.[18] No hydrogen atoms associated with the water molecules were located from the difference Fourier map. CSD-428009 (**2a**) contains supplementary crystallographic data for this paper. These data can be obtained free of charge from the Fachinformationszentrum Karlsruhe, 76344 Eggenstein-Leopoldshafen, Germany [fax, (+49)7247-808-666; e-mail, crysdata@fiz-karlsruhe.de; web site, http://www.fiz-karlsruhe.de/request_for_deposited_data.html]. Crystallographic data are summarized in Table 2.

Table 2. Crystal Data and Structure Refinement of Compound 2a

formula	$Na_{12}[H_{24}\{Nb_4O_6(OH)_4\}\{Nb_6P_2W_{12}O_{61}\}_4]\cdot 24H_2O$
empirical formula	$Na_{12}H_{76}Nb_{28}P_8W_{48}O_{278}$
formula wt, g mol^{-1}	16473.8
cryst syst	monoclinic
space group	$C2/c$
a, Å	44.907(12)
b, Å	31.328(9)
c, Å	25.536(7)
β, deg	92.954(6)
V, $Å^3$	35878(17)
Z	4
D_c, g cm^{-3}	3.044
μ, mm^{-1}	16.311
F_{000}	28880
cryst size, mm^3	0.37 × 0.29 × 0.26
θ range for data collection, deg	1.67−25.00
reflns collected/unique	92545/31558
R_{int}	0.1560
goodness-of-fit on F^2	1.013
R1,[a] wR2[b] [$I > 2\sigma(I)$]	0.0796, 0.1784
R1,[a] wR2[b] (all data)	0.1905, 0.2052

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$.

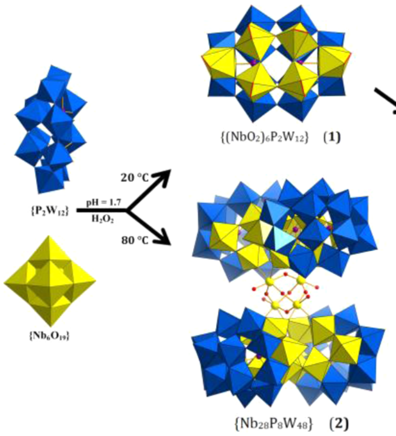
Biological Materials and Methods. *Cell Culture and MTT Assay.* The MCF-7 (human breast cancer), HCT-116 (human colon cancer), and BEL-7402 (human hepatoma cancer) cell lines were purchased from the Shanghai Institute for Biological Science, Chinese Academy of Sciences (Shanghai, China), and supplemented with 1 mM glutamine and 10% (v/v) fetal calf serum. Cells were cultured at 37 °C under a 5% CO_2 atmosphere. The antiproliferative ability of the compounds was evaluated in MCF-7, HCT-116, and BEL-7402 cells by the conversion of MTT to a purple formazan precipitate as previously described. Cells were seeded in 96-well plates at 5 × 10^3 cells $well^{-1}$. After 12 h, various concentrations (1, 5, 10, 30, and 50 μM) of compounds **2a**, $\mathbf{P_2W_{12}}$, and $\mathbf{Nb_6O_{19}}$ were subsequently added and incubated for 48 h. The inhibition rate was calculated from plotted results using untreated cells as 100%.

■ RESULTS AND DISCUSSION

Synthesis. Given the fact that the formation of polyanions depends more on the reaction conditions than on the type of polyanion precursors used, it is possible to extend the family of **1** using a combination of components, pH, and temperature control assembly. As shown in Scheme 1, the title polyanion could be formed from the composing materials instead of the preformed **1**, as in the case of the reported Keggin-based POMs.[7,8] It is well-known that $\mathbf{P_2W_{12}}$ is a metastable precursor that easily transforms in aqueous solution to other Wells−Dawson derivatives, with a strong dependence on the pH.[3,4a,b,e,19] However, after the incorporation of six niobium ions, the more stable synthon **1** is formed, which is present in **2**.

Interestingly, the synthetic conditions for **1** and **2** are very similar, and the reagents used are identical (Scheme 1).The key factors determining whether **1** or **2** is formed appear to be the

Scheme 1. Synthetic Routes Leading to the Isolation of Polyanions 1 and 2



pH and temperature. This work demonstrates that small changes in the synthetic conditions can have large consequences with respect to the product formed. The following points are very important for ensuring reproducibility. In the synthetic procedure, $\mathbf{P_2W_{12}}$ must be added quickly after the complete addition of a HCl_{aq} solution; otherwise, a cloudy solution will be obtained, indicating decomposition of $[Nb_6O_{19}]^{8-}$.[8a] If the reaction is performed without a pH change at 20 °C for 2 h, the bright-yellow color of the starting mixture is maintained, and **1** is the major product. A slight color change of the solution after heating suggests that the peroxo groups may be partially decomposed thermally, which is reminiscent of the transformation from $[(NbO_2)_3GeW_9O_{37}]^{7-}$ to $[Nb_3GeW_9O_{40}]^{7-}$.[8a] Also, **2** could be obtained with heating at 80 °C until the solution turned colorless, indicating the formation of peroxo-free intermediate $[Nb_6P_2W_{12}O_{62}]^{12-}$ $[Nb_6P_2W_{12}$ (**3**)]. On the other hand, polyanion **2** can be crystallized without the need for cesium ions. This is in contrast to the original report indicating an essential templating role of Cs^+ in the formation of Keggin-based analogues.[7,8]

Structure of the Polyanion. The solid-state structure of **2** shows a gigantic Nb_{28}-containing 48-tungsto-8-phosphate (Figure 1), comprising two $[P_4W_{24}Nb_{12}O_{122}]^{20-}$ dimeric units, rotated 180° with respect to each other and connected by four Nb−O−Nb bridges, resulting in an adamantane-like $\{Nb_4O_6\}$ core. The adamantanoid unit is very common in 3d TMSPs, such as $\{Mn_4O_6\}$,[20] $\{Co_4O_4\}$,[16h,21] $\{Ni_4O_6\}$,[22] and $\{Fe_4O_6\}$[23] and in three niobium-substituted Keggin-based polyanions.[7d,8] However, the latter three consist four Keggin units unlike four Wells−Dawson units in **2**, which is a great addition to polyoxoniobate chemistry.

In particular, the two symmetrically related half-units $[Nb_6P_2W_{12}O_{62}]^{12-}$ (Figure S1 in the Supporting Information) are fused via two parallel, equatorial Nb−O−Nb bridges (Figure 2). Such dimerization through Nb−O−Nb bridges has so far only been observed for the aforementioned niobium-substituted Keggin anions.[6,7a,c,8] We now present, for the first time, the synthesis and structure of a Nb−O−Nb-linked Dawson tetramer. Polyanion **2** is structurally related to the tetrameric Keggin-based polyanions $[Nb_4O_6(Nb_3SiW_9O_{40})_4]^{20-}$,[7d] $[Nb_4O_6(Nb_3GeW_9O_{40})_4]^{20-}$,[8a] and $[Nb_4O_6(Nb_3AsW_9O_{40})_4]^{16-}$.[8b]

Alternatively, **2** can be viewed as four $\mathbf{P_2W_{12}}$ fragments supporting an unprecedented $\{Nb_{28}\}$ cluster (Figure 3), with

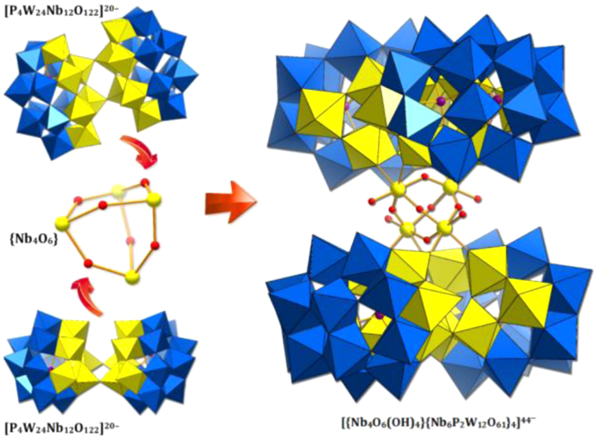


Figure 1. Combined polyhedral/ball-and-stick representation of the various building blocks comprising polyanion **2**. All cations and crystal water molecules are omitted for clarity. Color code: WO_6, blue polyhedra; NbO_6, yellow polyhedra; Nb, yellow balls; P, purple balls; O, red balls.

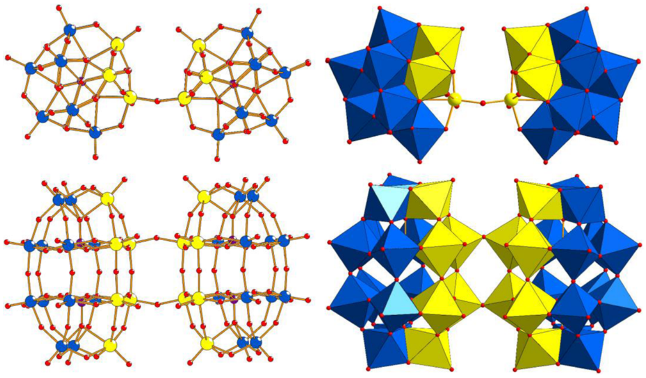


Figure 2. View from different directions of the combined polyhedral/ball-and-stick representation of the $[P_4W_{24}Nb_{12}O_{122}]^{20-}$ dimeric unit. All cations and crystal water molecules are omitted for clarity. Color code: WO_6, blue polyhedra; NbO_6, yellow polyhedra; Nb, yellow balls; P, purple balls; O, red balls.

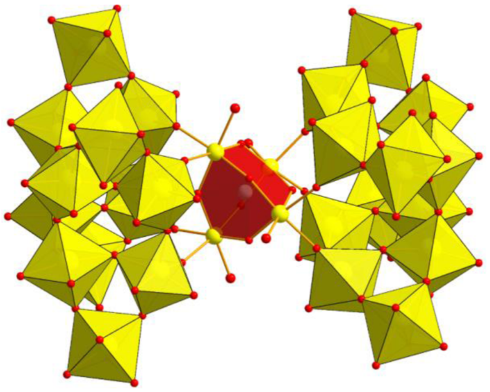


Figure 3. Representation of the unprecedented $\{Nb_{28}\}$ cluster in polyanion **2**.

the maximum nuclearity of niobium observed in niobium-substitued POM chemistry. With regard to the substituted Wells−Dawson clusters, only a few tetrameric structures have been characterized, such as the iron-substituted derivatives $\{Fe_{27}P_8W_{49}\}$[23] and $\{Fe_{12}(P_2W_{15})_4\}$,[24] the titanium-substituted derivatives $\{Ti_{12}(P_2W_{15})_4\}$[25a,b] and $\{Ti_{16}(P_2W_{15})_4\}$,[25c,d] the cobalt-substituted derivative $\{Co_{14}(P_2W_{15})_4\}$,[26] and the nickel-substituted derivative $\{Ni_{14}(P_2W_{15})_4\}$.[27] Of all of these species, only for $\{Fe_{27}P_8W_{49}\}$ is the hexalacunary $\mathbf{P_2W_{12}}$ fragment maintained.[23]

It is worth noting that polyanion **2** resembles structurally the $\{Fe_{27}P_8W_{49}\}$ cluster of Gouzerh and co-workers.[23] In the latter, the substituted metal is Fe^{III}, and each of the four $Fe_6P_2W_{12}$ subunits is connected by three Fe—O—Fe bridges to the $\{Fe_4O_6\}$ core. Both polyanions **2** and $\{Fe_{27}P_8W_{49}\}$ contain four $M_6P_2W_{12}$ Dawson units linked by an $\{M_4O_6\}$ adamantine core. Despite the fact that $\mathbf{P_2W_{12}}$ is metastable, both polyanions have retained this entity throughout the synthetic process. Moreover, in $\{Fe_{27}P_8W_{49}\}$, two $\mathbf{P_2W_{12}}$ units are linked by three Fe—O—Fe bridges involving the three outer iron atoms. However, in **2**, the substituted metal is the larger Nb^V ion. Each of the four $Nb_6P_2W_{12}$ subunits is connected by two Nb—O—Nb bridges to the $\{Nb_4O_6\}$ core, and they are linked to pairs by two parallel Nb—O—Nb bridges. Furthermore, 28 niobium atoms are embedded among four P_2W_{12} units in **2**, whereas the nuclearity of iron in $\{Fe_{27}P_2W_{49}\}$ is 27, rendering the former as the largest transition metal containing $\mathbf{P_2W_{12}}$-based POM characterized so far.

Bond valence sum (BVS) calculations for **2** are consistent with tungsten and niobium being in the 6+ and 5+ oxidation states, respectively.[28] In addition, four monoprotonated oxygen atoms were identified for **2**, indicating an $[Nb_4O_6(OH)_4]^{4+}$ core (Figure S2 in the Supporting Information). Charge-balance considerations with countercations suggested that compound **2a** contains many protons, namely, $Na_{12}[H_{24}\{Nb_4O_6(OH)_4\}\{Nb_6P_2W_{12}O_{61}\}_4]\cdot 24H_2O$. As stated already by Bontchev and Nyman[29] and us,[16a] the very large number of crystallographically independent atoms and parameters prevented the direct location of protons from the Fourier maps. Thus, we think that the 24 protons in **2a** are probably delocalized, whereas 4 protons are localized.

IR Spectroscopy. The FTIR spectra of **2a**, **1**, and $K_6[\alpha\text{-}P_2W_{18}O_{62}]\cdot 14H_2O$ ($\mathbf{P_2W_{18}}$) are shown in Table 3 and Figure S6 in the Supporting Information. They all show strong and medium bands in the range of 1100−1000 cm^{-1}, associated with antisymmetric stretching of the P—O bond. The medium-to-strong bands at approximately 956, 907, and 773 cm^{-1} originate from the antisymmetric stretching vibrations of the terminal W═O bonds and the W—O—W bridges, respectively. This confirms that the Wells−Dawson-type heteropolytungstate framework remains intact under the condition of the synthesis, consistent with the formulation of **2a** as containing the monomeric polyanion **1**.

Table 3. Comparson of the IR Spectra for $\mathbf{P_2W_{18}}$, 1, and 2a

	ν(P−O)	ν(W═O), ν(W−O−W)	ν(O−O)	ν(Nb−O−Nb)
$\mathbf{P_2W_{18}}$	1091, 1021	960, 910, 782	none	none
1	1075, 1003	953, 906, 780	870	none
2a	1091, 1010	956, 907, 773	none	685

The significant changes in the IR spectra (Figure 4) of **2a** with respect to **1** are the disappearance of a weak intensity band at 870 cm^{-1} and the appearance of a strong intensity band at 685 cm^{-1}, which is characteristic of the antisymmetric stretching vibrations of peroxo groups[7d,30] and Nb—O—Nb bridges,[6,7a,d,8,31] respectively. This is in satisfactory agreement with the solid-state structure.

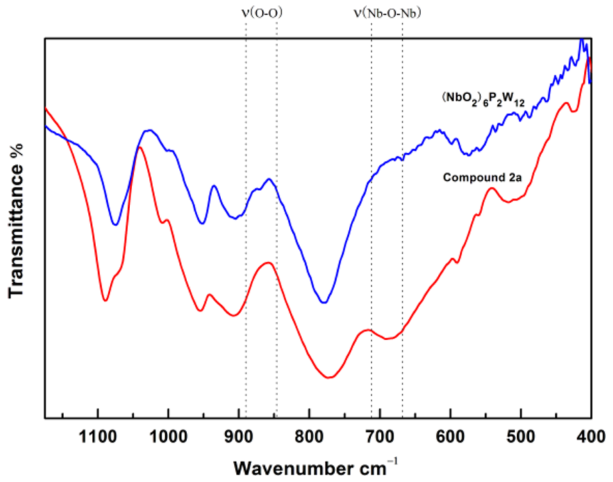


Figure 4. IR spectra of **2a** and **1** in the region between 1175 and 400 cm^{-1}.

Powder X-ray Diffraction (PXRD) Results. In order to check the phase purity of the title compounds, PXRD patterns of **2a** were performed on a Bruker D8 Advance powder X-ray diffractometer ranging from 5° to 50° at room temperature. However, the peak positions of the simulated and experimental PXRD patterns do not match well with each other (Figure S7 in the Supporting Information), which is probably due to solvent loss. On the other hand, the difference in the intensities of some diffraction peaks may be attributed to the preferred orientation of the crystalline powder samples.

Cell-Growth Inhibition. To determine whether **2a** has activity in the inhibition of tumor-cell growth, we screened compound **2a** against three tumor cell lines: MCF-7 (human breast cancer), HCT-116 (human colon cancer), and BEL-7402 (human hepatoma cancer). As shown in Figure 5, the comparative results show that **2a** could efficiently inhibit the growth of MCF-7 cells in a dose-dependent manner at **2a** concentrations of 1−50 μM. The inhibition rates of **2a** at 1, 5, 10, 30, and 50 μM on MCF-7 were measured as 12.42 ± 1.80%, 67.67 ± 2.84%, 75.25 ± 3.35%, 75.70 ± 3.37%, and 80.68 ± 2.27%, respectively (Figure S3 in the Supporting Information). The IC_{50} value against the MCF-7 cell line is 5.21 ± 0.46 μM, which manifests that **2a** has good activity against human breast cancer cells.

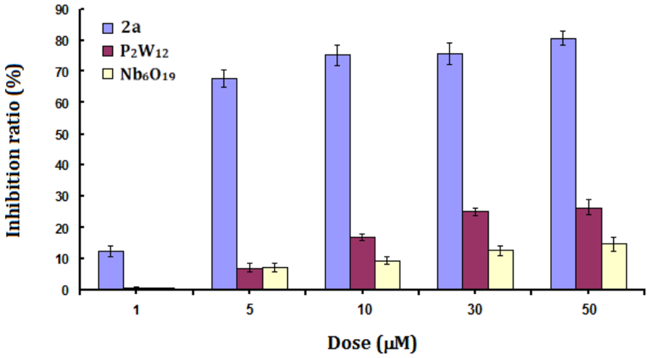


Figure 5. Column graphs of the inhibition ratios of **2a**, $\mathbf{P_2W_{12}}$, and $\mathbf{Nb_6O_{19}}$ against the MCF-7 cell line.

Moreover, we have also studied the activity of **2a** against HCT-116 and BEL-7402 cell lines, whereas the IC_{50} values of **2a** are about 22 and 54 μM in the HCT-116 and BEL-7402 cells, respectively (Table 4 and Figures S4 and S5 in the Supporting Information). A comparison of the inhibition rates of **2a** with those of the parent reagents $\mathbf{P_2W_{12}}$ and $\mathbf{Nb_6O_{19}}$ suggested that **2a** was significantly more active (Figure 5). It is likely that the main reason for the activity of **2a** is the $[\{Nb_4O_6(OH)_4\}\{Nb_6P_2W_{12}O_{61}\}_4]^{36-}$ cluster, with the niobium and tungsten ions having a synergic effect, as described recently for $\{PNb_8V_8\}$.[32] In conclusion, the observation that the niobium-substituted polyoxotungstate activity is obviously enhanced is of interest, suggesting that more niobium/tungsten mixed-addendum clusters may have much better activity.

Table 4. Cell-Growth Inhibition Assay Results for 2a Compared to the Parent Molecules

	IC_{50} (μM)[a]		
	MCF-7	HCT-116	BEL-7402
2a	5.21 ± 0.46	22.04 ± 2.56	>50
$\mathbf{P_2W_{12}}$	>50	>100	>100
$\mathbf{Nb_6O_{19}}$	>100	>100	>100

[a] IC_{50} values represent the concentration causing 50% growth inhibition. They were determined by the linear regression method. Each sample is the mean of three independent experiments.

■ CONCLUSION

In conclusion, the unprecedented tetrameric Nb_{28}-containing 48-tungsto-8-phosphate **2** has been synthesized. Polyanion **2** comprises 28 niobium centers and hence represents the first example of a niobium-core-based Wells–Dawson tetramer, and at the same time, **2** is the largest niobium/tungsten mixed-addendum POM cluster. The in vitro assays revealed that **2a** exhibits effective inhibition activity against human breast cancer MCF-7 cells. The observation that the niobium-substituted polyoxotungstate activity is obviously enhanced is of interest.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

X-ray crystallographic data in CIF format, Figures S1–S7, and BVS results of all of the oxygen atoms on polyanion **2** (Table S1). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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