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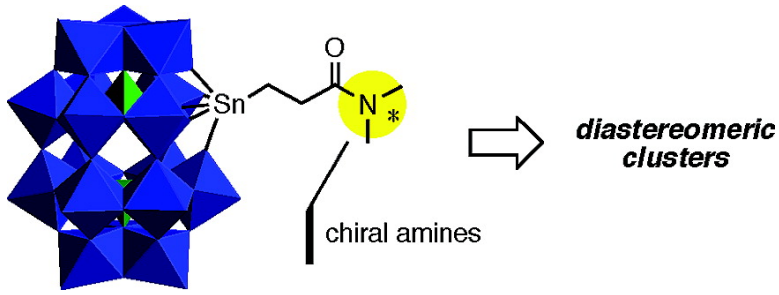
J. Am. Chem. Soc., **2005**, 127 (18), 6788-6794• DOI: 10.1021/ja050397c • Publication Date (Web): 16 April 2005



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Efficient Preparation of Functionalized Hybrid Organic/Inorganic Wells−Dawson-type Polyoxotungstates

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Contribution from the Laboratoire de chimie inorganique et matériaux moléculaires (UMR CNRS 7071) and Laboratoire de chimie organique (UMR CNRS 7611), Université Pierre et Marie Curie, 4 place Jussieu, 75005 Paris, France

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Abstract: Hybrid organic/inorganic Wells−Dawson polyoxotungstates have been prepared through addition of functionalized tricholorostannanes to lacunary α_2- and α_1-$[P_2W_{17}O_{61}]^{10-}$. Coupling of amines and alcohols to polyoxotungstate platforms led to new structures in good yields. Coupling of chiral amines to the previously unknown organotin-substituted α_1 derivatives allowed the isolation of diastereomers, which feature in some cases split ^{1}H, ^{13}C, and ^{31}P NMR spectra. This is the first example of NMR observation of a single pair of diastereomers in the α_1-Wells−Dawson series. It opens the way to potential resolution of those chiral polyoxotungstates.

Polyoxometalates (POMs) are a large family of metal−oxygen clusters of the early transition metals in high oxidation states, most commonly V^V, Mo^{VI}, and W^{VI}.[1] Their diversity in structure and composition allows a wide versatility in terms of shape, polarity, redox potentials, surface charge distribution, acidity, and solubility, which appeals to the chemical community at large.

The elaboration of POM-based molecular materials is an evolving field of research due to the intrinsic electronic and optical properties of many POMs. The introduction of organic moieties into these materials allows the development of organic−inorganic hybrid materials.[2] The last 20 years have witnessed a growing interest in the biological properties of POMs and their potential applications in medicine.[3] POMs exhibit antiviral, notably anti HIV,[4] as well as antitumor[5] and antibiotic[6] activities.

The introduction of organic groups is an efficient way to greatly increase the number of compounds available, and thus to expand their properties.[7] For example, derivatization of POMs can result in activation of the surface oxygen atoms.[8] On the other hand, the electronic properties and/or bulk of the POM may modify the properties of the side chains.[9] Ligands with an especially designed functionality can be used to achieve assembly of POM units. Complex networks with selected properties would result from this approach.[10] Finally, in addition to opening the way to a vast number of new structures to be screened for bioactivity, introduction of organic groups onto the POM frameworks might modulate essential features, such as stability, bioavailability, and recognition, that need to be mastered for pharmaceutical purposes.[3a]

As a consequence, a significant number of organic/inorganic hybrid POMs and specific methodologies to obtain them have been reported.[7] However, most of them are limited to very simple organic moieties, and there have been only scattered reports on the reactivity of the side chain.[10b,11] A notable contribution has been recently provided by Neumann who prepared salen-type ligands through imination of amino groups grafted on Keggin POMs.[9a] Many organically derivatized POMs are unstable in water. Starting from hydrolytically more stable cyclopentadienyltitanium-substituted POMs, Keana reported the preparation and reactivity of derivatives with various functional groups.[11a−c] We decided to reexamine the heteropolytungstates α_2-$[P_2W_{17}O_{61}(SnR)]^{7-}$ reported by Pope.[12] The combination of

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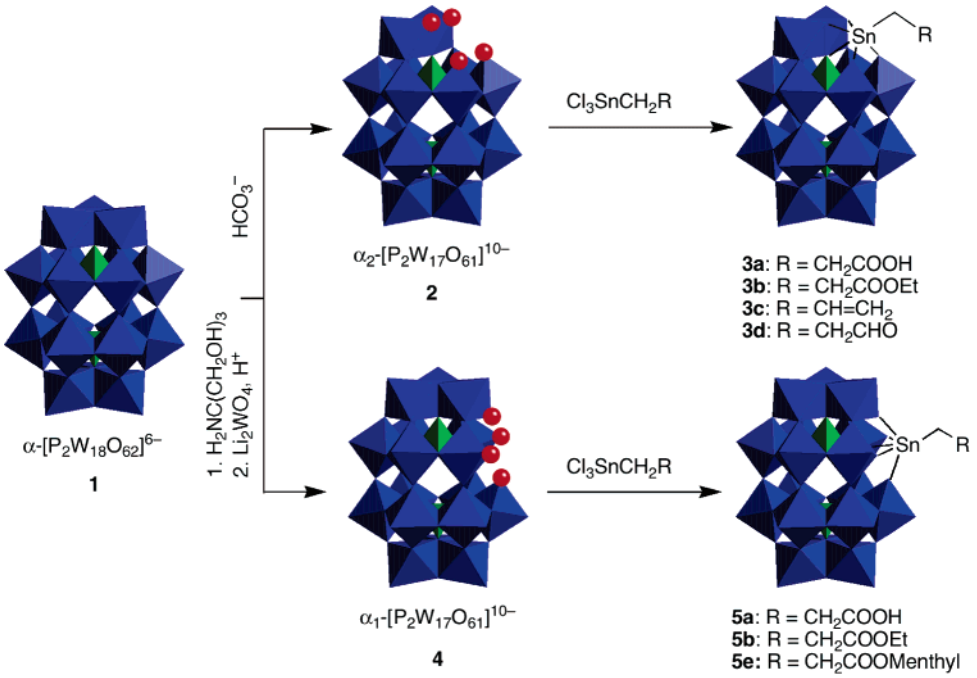
10.1021/ja050397c CCC: $30.25

Scheme 1. Preparation of Functionalized Wells−Dawson Polyoxotungstates



monoorganotin compounds with monolacunary POMs allows the introduction of only one organic group, whereas the use of monoorganosilicon derivatives yields POMs with two RSi groups such as α_2-$[P_2W_{17}O_{61}\{(RSi)_2O\}]^{6-}$.[13] Several monoorganotin groups can be complexed by multilacunary POMs.[14] Diorganotin derivatives have been reacted with polylacunary POMs to yield complexes with multiple organic side chains.[15] Most recently, Kortz has obtained 2D materials and a giant POM architecture from dimethyltin derivatives and trilacunary (AsW_9O_{33}) fragments.[9−16]

The heteropolytungstate compounds have promising antitumor activities,[17] but the organic groups that were introduced were very simple and did not allow further functionalization. Also, no such compounds had been reported in the α_1 series. We decided to focus on a versatile strategy relying on the coupling of highly functionalized organic molecules to keystone hybrid structures. We report herein the results we gathered following this flexible strategy.[18]

Preparation of Functionalized Wells−Dawson Polyoxotungstates. Pope reported the synthesis of α_2-$[P_2W_{17}O_{61}(SnR)]^{7-}$ by two routes: the first option relies on alkylation of tin(II) compound α_2-$[P_2W_{17}O_{61}Sn]^{8-}$ by 1-bromododecane.[12b] The Sn(II) compound is very prone to oxidation to the Sn(IV) polyanion, as Pope had reported. We thus decided to follow the second strategy and obtain the desired polyanions by treating different $RSnCl_3$ with monovacant α_2-$[P_2W_{17}O_{61}]^{10-}$ **2**[11e,12a,19] or α_1-$[LiP_2W_{17}O_{61}]^{9-}$ **4** (Scheme 1 and Table 1).

Following Pope's procedure, treatment of a buffered (pH = 5.3, c = 0.2 M) aqueous solution of $K_{10}\alpha_2$-$[P_2W_{17}O_{61}]$ **2**[20] with $Cl_3Sn(CH_2)_2CO_2H$[21] yielded a new anion. Addition of tetrabutylammonium bromide (TBABr) precipitated a white solid, whose IR spectrum showed the vibrational bands arising from the Wells−Dawson structure without the typical splitting of the P−O stretching vibration in the lacunary compound, thus indicating that the lacuna had been filled. ^{31}P NMR analysis showed the presence of a single product with two nonequivalent phosphorus atoms (δ = −12.7 and −9.7 ppm). The high-frequency resonance consists of a single line flanked by a pair of satellites arising from unresolved coupling with ^{117}Sn and ^{119}Sn (J = 27.5 Hz). Consequently, the tin atom is bound to the phosphate group. ^{1}H NMR confirms the presence of the side chain, thus showing unambiguously that we succeeded in preparing α_2-$[P_2W_{17}O_{61}\{Sn(CH_2)_2CO_2H\}]^{7-}$ **3a** in good yield (entry 1). The same method allowed the preparation of α_2-$[P_2W_{17}O_{61}\{SnCH_2CH{=}CH_2\}]^{7-}$ in comparable yield (73%, entry 4).

Unfortunately, attempts to prepare the α_1-isomer **5a** using the same method led to isomerization to the α_2-isomer. This prompted us to find a modified procedure. We therefore developed a new synthesis relying on a solid to organic phase transfer. In this process, the lacunary POM was suspended in a solution of TBABr in acetonitrile. The trichlorostannane was added to the mixture and provided us with clean **5a** after 1 h (95%, entry 7). To the best of our knowledge, this was the first hybrid α_1-Wells−Dawson polyoxotungstate ever reported. The relative mildness of the latter method and the easier workup led us to introduce it to the α_2 series. Following method B, **3a**

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(17) Wang, X.-H.; Liu, J.-F. *J. Coord. Chem.* **2000**, *51*, 73−82. See also ref 3b.
(18) A preliminary report of this work has been published as a communication. See: Bareyt, S.; Piligkos, S.; Hasenknopf, B.; Gouzerh, P.; Lacôte, E.; Thorimbert, S.; Malacria, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 3404−3406.
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Table 1. Preparation of Functionalized Polyoxotungstates

entry	S.M.	R	method[a]	prod.	yield (%)
1	**2**	CH_2CO_2H	A	**3a**	83
2	**2**	CH_2CO_2H	B	**3a**	90
3	**2**	CH_2CO_2Et	B	**3b**	89
4	**2**	$CH{=}CH_2$	A	**3c**	73
5	**2**	CH_2CHO	B	**3d**	68[b]
6	**4**	CH_2CO_2H	A		—[c]
7	**4**	CH_2CO_2H	B	**5a**	95
8	**4**	CH_2CO_2Et	B	**5b**	92
9	**4**	CH_2CO_2Menth	B	**5e**	—[d]

[a] Method A: reaction run in water. Method B: solid/organic phase transfer. See Experimental Section for details. [b] Yield calculated from acrolein (two steps). [c] Partial isomerization to α_2-derivative **3a** was observed. [d] Desired hybrid polyanion **5e** was observed by ^{31}P NMR, but decomposed upon concentration.

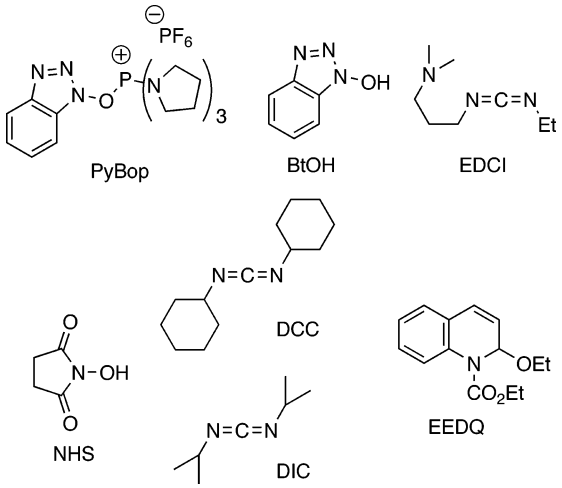


Figure 1. Coupling agents used during this work.

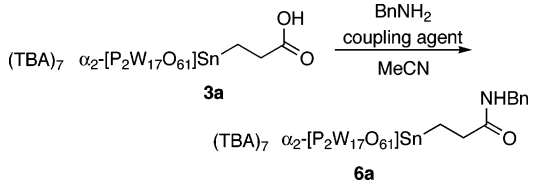
was obtained in 90% yield (entry 2). An additional key feature of this preparation is that the previously required acetate buffer is not needed. As a consequence, one can thus avoid employing acetic acid, which tends to stick to the polyoxotungstate framework and makes the purification quite cumbersome. Method B proved reasonably versatile, as it allowed formation of ester (entries 3, 8, and 9) and aldehyde (entry 5) derivatives in good yield, but not amides. The α_1-menthyl ester was observed by NMR, but decomposed upon concentration.

Coupling to α_2-Hybrid 3a. As our objective was to use the POM's "arm" as a linker, we sought conditions that would enable us to attach various molecules to the acid moiety. This task implies finding particularly efficient conditions, POMs with different side chains are almost impossible to separate, without creating cationic byproducts leading to scrambling of the counterions, which causes solubility and purity problems.

We selected seven types of activating systems, which we applied to the coupling of scaffold **3a** with benzylamine (Figure 1 and Table 2).

Oxalyl chloride led to immediate decomposition of the polyoxotungstate (entry 1), presumably through activation of a tungsten−oxygen bond. Upon using PyBop,[22] the starting polyanion was totally consumed after 14 h (entry 2). Both the IR and ^{31}P spectra indicated a plenary Wells−Dawson structure with a tin atom filling the α_2 lacuna. However, no proton signals other than those of the TBAs were present. The organic side

Table 2. Amide Formation Starting from Polyoxotungstate **3a**



entry	coupling agent	temp (°C)	yield (%)
1	$(COCl)_2$, DMF cat.	0	—[a]
2	PyBop, dark	room temp	
3	EDCI, BtOH	room temp	60[b]
4	DIC, NHS	room temp	56[b]
5	DCC, NHS	room temp	42
6	EEDQ	reflux	84
7	$ClCO_2i$-Bu, *t*-BuOK	0	88

[a] Degradation occurred. [b] One equivalent of the corresponding urea was associated to the polyanion.

chain had apparently been severed from the cluster by a retro-Michael-type cleavage of the Sn−C bond. We then turned our attention to activation of the carboxylic end by carbodiimide derivatives. Both EDCI/BtOH[23] and DIC/NHS[24] systems gave the desired product in acceptable yields (entries 3 and 4). Unfortunately, the urea byproducts remained so tightly associated to the polyoxotungstate, presumably via H-bonds, that they could not be separated from it. As we wanted to have pure **6a**, we switched to DCC, reasoning that the lower solubility of dicyclohexyl urea in acetonitrile could help its removal. This was the case, but some of the desired product was lost during the filtration (entry 5). Switching to EEDQ-mediated processes proved rewarding.[25] The yield in **6a** was excellent (84%, entry 6). This method has some valuable advantages: the sole byproducts are easy-to-remove ethanol and quinoline. Yet, it requires heating. We wanted to have a milder method to achieve our goal. As stated above, we believe that carbonylation of a tungsten−oxygen bond is at the root of the $(COCl)_2$/DMF-initiated decomposition of starting **3a**. Maybe switching to a less electrophilic system could hamper this side reaction. We thus decided to use $ClCO_2i$-Bu as activating partner, and *t*-BuOK as base. It turned out that this was highly beneficial, provided the amount of base was carefully monitored and limited to 1.5 equiv. As a base, *t*-BuOK is potentially harmful to POMs, but we took advantage of the fact that it is not soluble in acetonitrile, and thus less prone to decompose the cluster, while reactive enough to abstract the proton produced during the coupling. Indeed, solvents in which *t*-BuOK is soluble, such as DMF or DMSO, witnessed rapid decomposition of the POM. Most importantly, the reaction in acetonitrile could be carried out at 0 °C in excellent yield (88%, entry 7). As a consequence, we had two sets of conditions in hand. We endeavored to determine their scope and limitations (Table 3).

All EEDQ reactions were carried out in refluxing acetonitrile. Primary and secondary amines led to the corresponding amides in high yields (entries 1, 3). As stated before, switching to the chloroformiate-mediated coupling proved rewarding, because conversion of **3a** to **6a** and **6c** was much more rapid and took

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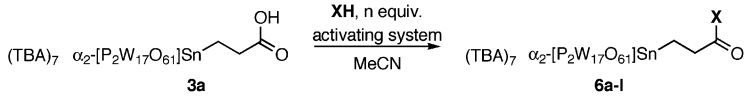
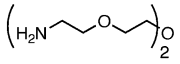
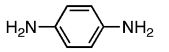
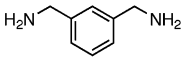
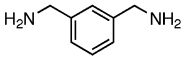
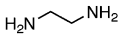
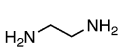
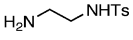
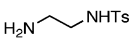
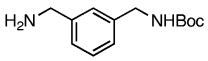
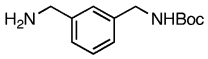
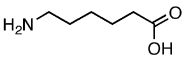
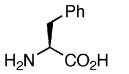
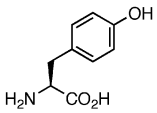
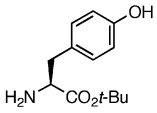
(25) Belleau, B.; Malek, G. *J. Am. Chem. Soc.* **1968**, *90*, 1651−1652.

Table 3. Scope and Limitations of Coupling to POM **3a**

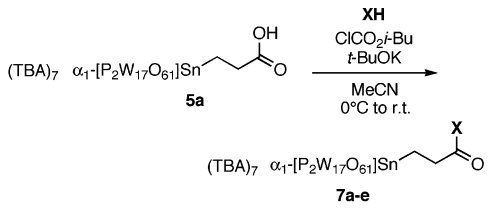


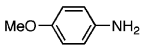
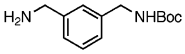
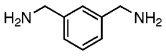
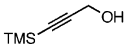
Entry	XH	n	Method[a]	t (h)	Product, Yield (%)
1	$BnNH_2$	3	C	4	**6a**, 84
2	$BnNH_2$	3	D	1.25	**6a**, 88
3	Bn_2NH	2	C	8	**6b**, 90
4	piperidine	2	D	1	**6c**, 57
5		6	C	140	**6d**, 70
6		6	C	120	**6e**, 66
7		3	C	70	**6f**, 66
8		3	D	2	-[b]
9		7	C	120	-[c]
10		3	D	2	-[d]
11		3	C	96	**6g**, 85
12		3	D	1.5	**6g**, 57
13		3	C	70	**6h**, 69
14		3	D	1.5	**6h**, 91
15		3	C	36	**6i**, 50
16		1.5	D	1.5	**6j**, 61[e]
17		3	C or D	-	-[f]
18		3	C	36	**6k**, 90
19	BnOH	2	C	12	**6l**, 86

[a] Method C: EEDQ-mediated coupling. Method D: chloroformiate-mediated coupling. See Experimental Section for details. [b] **6f** (30%) was isolated together with twice-coupled amine (20%) and several degradation products. [c] Maximum conversion was 80%; rapid degradation followed. [d] See text for details. [e] The amino acid was converted to its aminocarboxylate form prior to use. [f] No reaction occurred (method C); conversion to the aminocarboxylate form led to degradation (method D).

place at room temperature (entries 2, 4). This pattern was further illustrated by the coupling of monotosyl-ethylenediamine and mono-Boc-protected xylylenediamine (entries 11−14). In both cases, method D proved much more efficient and allowed the

Table 4. Scope and Limitations of Coupling to POM **5a**

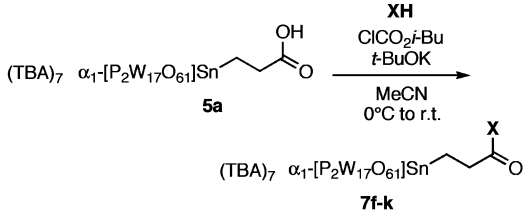


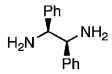
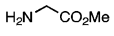
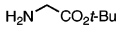
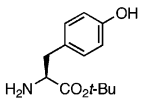
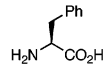
Entry	XH	t (h)	Product, Yield (%)
1	$BnNH_2$	1	**7a**, 73
2	Bn_2NH	1	**7b**, 64
3	*i*-Pr_2NH	1.25	**7c**, 41
4		1.25	**7d**, 46
5		1.25	**7e**, 76
6		1.5	-[a]
7	BnOH	1.5	no evolution
8		1.5	no evolution

[a] Desired POM was accompanied by large amounts of decomposed products and could not be isolated pure.

formation of the desired products without noticeable degradation of the POM framework. This could be observed by comparing the time needed to reach completion, as monitored by ^{31}P NMR. The isolated yields can be misleading because of the precipitation step. Reactions of diamines, whether dialkyl- or diaryl-, proved surprisingly much more difficult (entries 5−10). Following method C, longer reaction times were required to produce the aminoamides. When ethylenediamine was used, the reaction never reached completion: beyond 80% conversion, degradation progressed rapidly (entry 9). Protonation of ethylenediamine presumably took place, shut down the reaction, and eventually led to the decomposition of the cluster. Switching to method D was not beneficial. A 3:1 mixture of the desired product together with an unidentified polyoxotungstate was obtained in low yield (<40%). Overall, method D in not suited for diamines (compare entries 7 and 8). Acid, ester, and phenol moieties are tolerated (entries 15−18). Simple α-amino acids failed to give any amide through method C (no conversion observed, entry 17). However, it seems that the length of the spacer plays a role, because the reaction worked with other amino acids (entry 15). Deprotonation of the zwitterionic form to the α-aminocarboxylate led to rapid decomposition in the case of tyrosine, which bears an additional acidic proton, but was rewarding for phenylalanine (entry 16). C-Terminus protection of tyrosine greatly improved method C and triggered a nearly quantitative reaction (entry 18). Last, esters could be prepared via method C (entry 19), but not via method D. The previous table clearly demonstrates that methods C and D are complementary and have a broad joint scope, with some few limitations.

Table 5. ^{31}P NMR Behavior of Diastereomeric α_1-Polyoxotungstates



Entry	XH	Prod., yield (%)	^{31}P-NMR behavior
1		**7f**, 66[a]	no splitting
2		**7g**, 84	10 Hz splitting (P2)
3		**7h**, 63	no splitting
4		**7i**, 87	no splitting
5		**7j**, 71	10 Hz splitting (P1)
6[b]		**7k**, -[c]	11 Hz splitting (P2)

[a] Amide **7f** was isolated together with 6% of dealkylated product. [b] Phenylalanine must be deprotonated to the aminocarboxylate form. [c] Compound could not be isolated (50% pure).

Coupling to α_1-Hybrid 5a. We then decided to look for the coupling of α_1-derivatives (Table 4). Reaction of **5a** with benzylamine following the EEDQ procedure failed, leading to only 50% of the desired amide **7a**, accompanied by several α_2-byproducts (among which roughly 20% of **6a**). Reasoning that this was due to the well-known thermal isomerization of α_1 to α_2 POMs,[26] we switched to the milder chloroformiate procedure. Gratifyingly, coupling of **5a** with benzylamine yielded 73% of **7a** (entry 1). Two side products were observed when the reactions were not carried out with all of the due precautions. The first featured a complete structure displaying an Sn−P coupling. We did not try to isolate it, but its formation was tentatively attributed to a retro-Michael-type reaction. The second byproduct did not show this characteristic NMR pattern, and its ^{31}P NMR spectrum was identical to that of lacunary α_1 POM. The enhanced fragility of **5a** is probably responsible for those observations. We subsequently studied the scope of the coupling. The reaction was less general than in the α_2 series. Neither alcohols nor diamines worked. This does not come as a great surprise because those molecules required the EEDQ procedure, which is not suitable in the α_1 series. Yet, the reaction proved versatile enough with standard amines and monoprotected diamines. It should be once again pointed out that the reaction is much less tolerant to variations of the established experimental procedure. Such variations triggered immediate

(26) (a) Contant, R.; Hervé, G. *Rev. Inorg. Chem.* **2002**, 22, 63−111. (b) Contant, R.; Richet, M.; Lu, Y. W.; Keita, B.; Nadjo, L. *Eur. J. Inorg. Chem.* **2002**, 2587−2593.

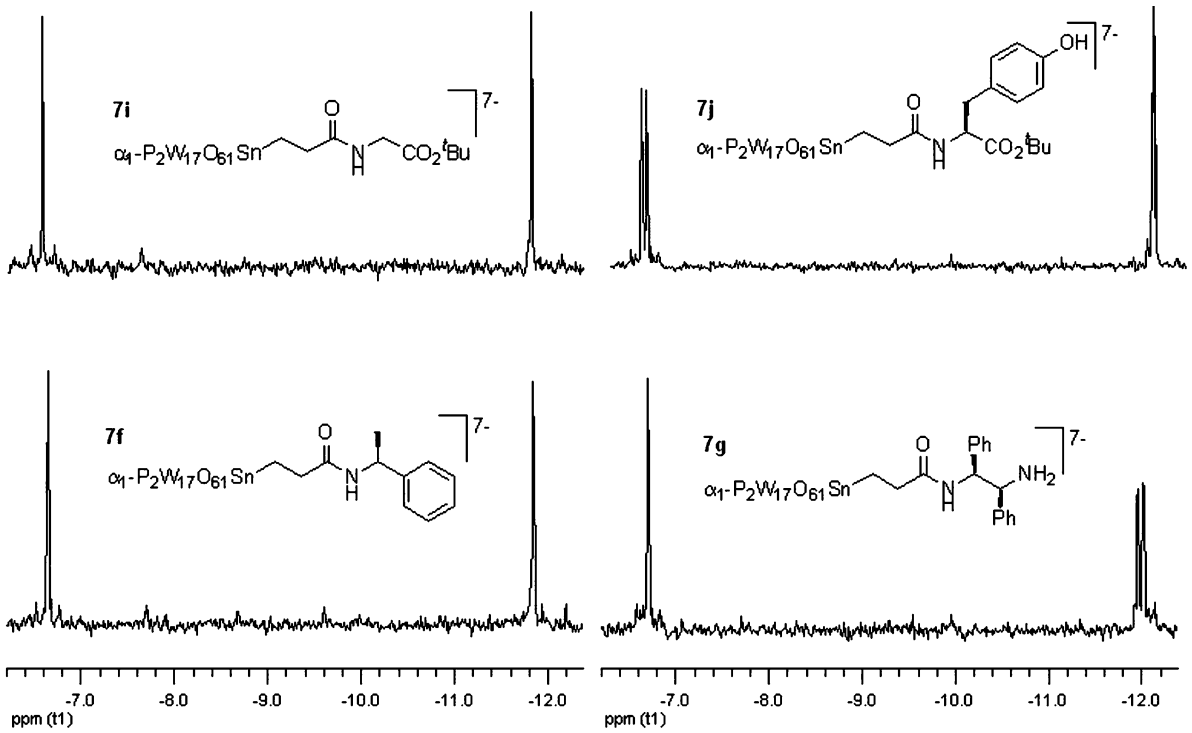


Figure 2. ^{31}P signals for clusters **7f**,**g** and **7i**,**j**.

formation of the lacunary α_1-byproduct. Nevertheless, loss of tin could be circumscribed to less than 5% (NMR detection limit), provided that the reaction time was closely monitored.

Toward the Resolution of Chiral α_1-Wells−Dawson Polyoxotungstates. As stated before, α_1-Wells−Dawson polyoxotungstates are chiral. Yet, the enantiomers have never been separated, despite the obvious potential importance of such an achievement. In a seminal article, Pope mentioned that "chirality that results from 'substitution' of metal atoms into otherwise achiral parent structures (...) is so subtle that it has not yet been possible to discriminate between enantiomers in solution, let alone to devise methods of resolution", and reported that complexation of α_1-$[CeP_2W_{17}O_{61}]^{7-}$ by L-proline in water resulted in splitting of the ^{31}P NMR signals.[27] This breakthrough was no doubt made possible by the NMR shifts induced by the lanthanide. However, because the signals are an average of all of the coordination complexes around the lanthanide, for which both the polyoxometalate and the L-proline are ligands,[28] this approach might not be optimal for the resolution of the chiral POMs. We felt that our system could open the way to the formation of a pair of diastereomers by taking advantage of a covalent bond between POM **5a** and a chiral amine (Table 5).

α_1-Polyoxotungstate amide **7f** showed only two signals in ^{31}P NMR (entry 1). The phosphorus atom close to the tin (P1) showed a coupling with the tin atom, while the other phosphorus (P2) lacked such hyperfine structure. Coupling of **5a** with Corey's diamine yielded 84% of **7g**. To our great satisfaction, **7g** showed a split 1:1 signal for P2 (−12 and −11.9 ppm, Figure 2). To prove that those signals arose from the two diastereomers of the cluster, and not from an equilibrium between the two amide-bond rotamers, we designed several experiments (entries 3−6). In addition to the compounds shown in Table 4, two representative glycine esters failed to give any splitting, as one would expect because there is no stereogenic center on the side chain. Switching to tyrosine ester derivative **7j** reintroduces the splitting, but this time on P1 as evidenced by the coupling pattern. Eventually, phenylalanine hybrid **7k** featured a P2 splitting, but **7k** could not be isolated (entry 6). In all cases, the split signals were present in equal proportion, regardless of the deuterated solvent used (acetonitrile-d_3, DMSO-d_6, acetone-d_6). Furthermore, this proportion was modified neither through heating nor through cooling of an acetonitrile-d_3 solution of **7j** (−40 to 60 °C). This behavior is consistent with our hypothesis (the synthesis of the lacunary POM is a racemic process). Furthermore, it is unlikely that the rotameric equilibrium would not lead to a variation in the relative intensities.

Further circumstantial evidence can be obtained from comparing entries 4 and 5. Here again, it is unlikely that a simple addition of a phenyl ring should change the rotamer populations so dramatically (it would mean going from 100:0 to exactly 1:1). All things considered, this made us confident that we did observe α_1-Wells−Dawson polyoxotungstate diastereomers. To the best of our knowledge, this is the first direct observation of the two pure α_1-stereoisomers (that is, without averaging signals from different compounds).

We can draw from our study some hypotheses concerning the reasons for such an outcome. The amide side chain is probably folded to accommodate a hydrogen bond between the free amide proton and one of the negatively charged surface oxygen atoms of the POM (Figure 3). This possibility is also based on the number of examples in the literature, where POMs act as hydrogen-bond acceptors,[29] and on our own previous

(27) Sadakane, M.; Dickman, M. H.; Pope, M. T. *Inorg. Chem.* **2001**, *40*, 2715−2719.

(28) Luo, Q.-H.; Howell, R. C.; Dankova, M.; Bartis, J.; Williams, C. W.; Horrocks, W. D., Jr.; Young, V. G.; Rheingold, A. L.; Francesconi, L. C.; Antonio, M. R. *Inorg. Chem.* **2001**, *40*, 1894−1901.

(29) Johnson, B. J. S.; Schroden, R. C.; Zhu, C.; Young, V. G., Jr.; Stein, A. *Inorg. Chem.* **2002**, *41*, 2213−2218.

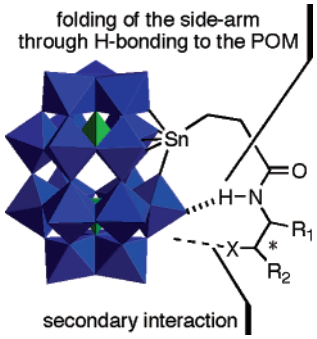


Figure 3. Possible model explaining the diastereomeric differentiation.

observation that one equivalent of urea remained generally attached to the POM framework when diimides were used as activating agents (see Table 2, entries 3, 4). As a consequence, it seems that splitting occurs when the folded side chain is able to allow for a second interaction with the polyanion, which brings the two stereogenic elements closer, and allow for the discrimination between the two POM configurations. In the case of Corey's diamine, the remaining amino group could be protonated to the ammonium. At the moment, we cannot anticipate (nor rationalize) which phosphorus atom will lead to a split signal. This clearly deserves more work, which is beyond the scope of this Article and will be presented in due course.

To conclude, we have devised efficient methods to prepare tin-substituted α_2- and α_1-Wells−Dawson polyoxotungstates using a high-yielding phase transfer procedure. Those complexes were not previously known in the α_1 series. We then were able to cleanly attach amines or alcohols to the side chains. This allowed us to access a variety of new structures, which could be used for several applications that we are currently pursuing. Eventually, we observed for the first time two diastereomeric α_1-Wells−Dawson POMs. We propose a rationale for such an outcome. Work toward establishing the scope of our method is being actively pursued. Better understanding of the way the splitting is made possible could help us devise new systems to separate the two diastereomers, which remains today an elusive challenge.

Experimental Section

General. Reagents and chemicals were purchased from commercial sources and used as received. Reactions were carried out under an inert gas, with magnetic stirring in redistilled solvents when necessary. Solvents were purified and dried by standard procedures. $K_{10}\alpha_2$-$[P_2W_{17}O_{61}]$ **2**, $K_9\alpha_1$-$[LiP_2W_{17}O_{61}]$ **4**, and $Cl_3Sn(CH_2)_2CO_2H$ were prepared as reported in the literature (see text). IR spectra were recorded in KBr pellets on a Biorad FTS 165 FT-IR spectrometer and with a Bruker Tensor 27 ATR diamant PIKE spectrometer. NMR ^1H, ^{31}P, ^{13}C spectra were recorded at 300, 121.5, 75.5 MHz, respectively, using a Bruker AC 300. Some ^1H, ^{31}P, ^{13}C NMR spectra were recorded at 400, 162, and 100 MHz using a Bruker ARX 400 and AVANCE 400. Chemical shifts are reported in ppm using, for ^1H and ^{13}C, solvent residual peak as internal references and H_3PO_4 as external references for ^{31}P. Coupling constants (*J*) are given in Hertz (Hz). C, H, and N elemental analyses were carried out by the Service Régional de Microanalyse de l'Université Pierre et Marie Curie and the Laboratoire Central d'Analyse du CNRS (Vernaison, France). K, P, Sn, and W were quantified by the Laboratoire Central d'Analyse du CNRS (Vernaison, France). The precision of the tunsgtene analyses is not always excellent, as is not unusual in the literature on polyoxotungstates.

General Procedure A (GPA). $Cl_3Sn(CH_2)R$ (0.5 mmol; 1 equiv) was added at room temperature to an aqueous potassium acetate buffered (pH = 5.3; 0.2 M; 100 mL) suspension of lacunar $K_{10}\alpha_2$-$[P_2W_{17}O_{61}]$ **2** (2.38 g; 0.5 mmol). After 10 min, the remaining solid was filtered off and the filtrate was treated with an aqueous solution (50 mL) of tetra-*n*-butylammonium bromide (TBABr, 1.67 g; 5 mmol; 10 equiv). The white precipitate was filtered and dried in vacuo, affording the desired tin-substituted POMs as white powders.

General Procedure B (GPB). $Cl_3Sn(CH_2)R$ (0.525 mmol, 1.05 equiv) was added at room temperature to a solution of TBABr (1.67 g; 5 mmol; 10 equiv) in acetonitrile (50 mL). Lacunar $K_{10}\alpha_2$-$[P_2W_{17}O_{61}]$ **2** (2.38 g; 0.5 mmol) or $K_9\alpha_1$-$[LiP_2W_{17}O_{61}]$ **4** (2.35 g; 0.5 mmol) was added, and the mixture was stirred for 1 h at room temperature under an argon atmosphere. The remaining solid was filtered off. Concentration of the solvent in vacuo afforded a pale yellow solid, which was recrystallized (EtOH/Et_2O 1:10) to give the desired tin-substituted POMs as a white powder.

General Procedure C (GPC). Polyoxotungstate $(TBA_6K)\alpha_2$-$[P_2W_{17}O_{61}SnCH_2CH_2CO_2H]$ **3a** (0.1 mmol; 1 equiv; 585 mg) was added to a solution of EEDQ (0.15 mmol; 1.5 equiv; 37 mg) in refluxing acetonitrile (10 mL). After 15 min, the amine was added to the solution. The mixture was refluxed until completion of the reaction, monitored by ^{31}P NMR. The solid was filtered off. Concentration of the solvent in vacuo afforded a pale yellow oil which was precipitated (acetone/Et_2O 1:10) to give the desired amide. This procedure could be scaled up to a 3 g scale (~0.5 mmol) without loss in yield.

General Procedure D (GPD). Polyoxotungstate $(TBA_6K)\alpha_2$-$[P_2W_{17}$-$SnCH_2CH_2CO_2H]$ (0.05 mmol; 1 equiv; 292 mg) or $(TBA_7)\alpha_1$-$[P_2W_{17}$-$SnCH_2CH_2CO_2H]$ (0.05 mmol; 1 equiv; 293 mg) was added to a suspension of freshly sublimed ^{t}BuOK (0.08 mmol; 1.5 equiv; 8 mg) in acetonitrile (5 mL) at room temperature. After 5 min, isobutyl chloroformate (0.08 mmol; 1.5 equiv; 10 μL) was slowly added at 0 °C (over 10 min). The reaction mixture was allowed to warm to room temperature for 30 min. The amine (*n* equiv) was then added to the vigorously stirred suspension. The mixture was stirred until completion of the reaction, monitored by ^{31}P NMR. The remaining solid was filtered off. Concentration of the solvent in vacuo afforded a pale yellow oil that was precipitated (acetone/Et_2O 1:10) to give the desired amide.

Acknowledgment. We gratefully acknowledge financial support from UPMC, CNRS, and Institut Universitaire de France, of whom M.M. is a senior member. S.B. thanks Prof. G. Béréziat and the Ministère de la Jeunesse, de l'Education Nationale et de la Recherche, for a fellowship.

Supporting Information Available: Analytical data for all new compounds, NMR spectra for compound **6c**, for which elemental analysis is lacking, and relevant spectra of the α_1-clusters showing splitting of the signals. This material is available free of charge via the Internet at http://pubs.acs.org.

JA050397C