Physicochemical Characterization of Polyvinyl Pyrrolidone: A Tale of Two Polyvinyl Pyrrolidones
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ABSTRACT: Of several samples of polyvinyl pyrrolidone (PVP) used to coat and stabilize freshly manufactured aqueous dispersions of silver nanoparticles, one batch gave anomalous results: the dispersion maintained continued stability, even on extensive dilution. Our efforts to understand this desirable feature concluded that the generally used spectral method of PVP purity verification, Fourier transform infrared (FTIR) spectroscopy, was incapable of answering our inquiry. This led to the employment of several other methods, including X-ray photoelectron and nuclear magnetic resonance spectrosopies, which ultimately revealed several possible reasons for the dilution stability, including incomplete PVP hydrolysis during manufacture and the presence of hydroperoxide contaminants. It led, as well, to explanations for the shortcomings of FTIR spectroscopy as a verification method for PVP purity.

INTRODUCTION
Polyvinyl pyrrolidone [in fact, poly(N-vinyl-2-pyrrolidone), PVP] is used in a vast number of medical, industrial, technological, pharmaceutical, food, cosmetic, and other applications. Having a yearly production of about 3 M tons,1 it is made by the free radical polymerization of N-vinyl-2-pyrrolidone2 and, like its monomer, is soluble in a large number of polar solvents, including water. While many free radical initiators and solvents may be used, PVP is generally produced in water using H2O2 as the initiator. This generates a polymer chain that is terminated on the one end by a hydroxyl group and on the other by a 2-pyrrolidone ring; in the final step, the latter is hydrolyzed to give free 2-pyrrolidone and an aldehyde chain termination.2

More recently, PVP has found an additional use, in the manufacture and stabilization of metallic nanoparticles (NPs) (e.g., Ag3−12). Such NPs are made by the reduction of aqueous metal salts in the presence of PVP, which coats them as they form, stabilizing them by preventing their contact and agglomeration and limiting their growth. The characterization of the envelopment of the NPs by PVP has been studied by many groups,3−12 almost exclusively by vibrational spectroscopy, with the general conclusion that the 2-pyrrolidone ring binds to the NP through reaction with the carbonyl to form an alkoxide

\[ >C = O + \text{metal} \rightarrow >C - O - \text{metal} \]  

(1)

This is apparently based entirely on the slight (∼10 cm⁻¹) shift of an IR peak, located at ∼1660 cm⁻¹ and attributed to the carbonyl stretch, when reacted with Ag NPs. However, a spectral shift of 10 cm⁻¹ (=0.120 kJ/mol = 0.00124 eV) is hardly enough to qualify for the bonding described in eq 1. The researchers cited in refs 3−12 appear not to have realized that the pyrrolidone ring is, in fact, a γ-lactam (i.e., a five-membered cyclic amide). Thus, as is well known,13 the amide group is hybridized, so that any shift in the frequency of the peak can just as easily be attributed to reaction at the N as at the C==O. Indeed, this is why, in the case of amides, the peak at 1660 cm⁻¹ is known as amide I rather than as a carbonyl stretch. Unfortunately, because we are dealing with a tertiary amide, there is no amide II peak at ∼1550 cm⁻¹ to help with the analysis. Our present study was motivated by an unexpected finding: except for one lot of PVP, all purchased in China, the aqueous dilution of freshly made Ag NP dispersions caused the eventual loss of dispersion stability; the PVP, washed off on dilution, permitted the NPs to aggregate and settle out of the previously uniform dispersion, thus confirming that no strong chemical bond (i.e., alkoxide) had formed between the Ag NP and PVP. The one anomalous lot did not aggregate even on extensive dilution. That anomalous lot, to which we refer as PVP-1, had several other distinctive features: (1) aqueous solutions (10−40 wt %) became increasingly yellow-tinged on standing and

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(2) on subsequent drying, the residue was not colorless and transparent as expected; rather, it was yellow, fragile, cracked, and opaque. Other lots purchased from the same supplier acted normally, as did all lots purchased from other distributors.

Our colleague’s interest in maintaining the stability of the Ag NPs on dilution has prompted us to inquire why only PVP-1 was successful in doing so. We characterized all lots using the techniques discussed here; except for PVP-1, all other lots gave experimentally identical results. We report on PVP-1 and compare it with one of the normally responsive lots, which we refer to as PVP-2. The results will also be of interest to those using PVP in pharmaceuticals.

**RESULTS**

**IR Spectra.** IR spectra were obtained for both PVP-1 and PVP-2 powders, as well as for both samples dissolved in water and subsequently dried. The spectra are seen in Figure 1.

![Figure 1. IR spectra of the samples.](image)

Several peaks are relatively simple to attribute, such as those at ~3400 cm\(^{-1}\) (O–H stretch), ~2900 cm\(^{-1}\) (C–H stretches), ~1645 cm\(^{-1}\) (amide I), and 1490–1420 cm\(^{-1}\) (C–H deformations). Two others, at ~1280 and ~1020 cm\(^{-1}\), have been attributed to N–C stretches; however, the second peak is found only in PVP-1, and the N–C stretch is reportedly not seen in tertiary amides.\(^{13}\)

When compared both before and after dissolution and drying, the spectra of PVP-1 and PVP-2 manifest slight differences, although there are no key spectral alterations of either PVP sample. That is, the act of dissolution and drying has changed nothing that is obvious from their IR spectra.

**X-ray Photoelectron Spectroscopy.** The X-ray photoelectron spectroscopy (XPS) spectra for PVP-1, both the original powder and the sample subsequent to dissolution and drying, can be seen in Figure 2; they were attributed using the NIST Photoelectron Spectroscopy Database;\(^{14}\) the attributions are found in Table 1. One notes that N1sB and O1sB appear only subsequent to dissolution and drying, signaling a new amide species, suggesting hydrolysis on aqueous dissolution.

Concerning PVP-2, the numbers and binding energies of peaks are similar to those for PVP-1 powder, as shown in Figure 2, and are similarly attributed in Table 1. There are no spectral changes to PVP-2 on dissolution and drying.

Our confidence in our attributions is supported by the following: each PVP repeat unit has a theoretical C/N/O ratio of 6:1:1. For the PVP-1 powder, the ratio of (C1sA + C1sB + C1sD)/(N1sA + N1sB)/(O1sA + O1sB) is 6:1:1, and, on dissolution and drying, it is 6:1:0.8. For PVP-2, it is 6:1:1.2.

**NMR Spectra.** The \(^1\)H NMR spectrum of a 20% solution of PVP-1 in D\(_2\)O (Figure 3) is compared with those of PVP-2 and a sample purchased from Sigma-Aldrich (S-A). Peak attributions for PVP are found in Table 2.

Clearly, the spectrum of PVP-1 differs markedly from those of PVP-2 and the S-A sample, which appear to be identical. Several peaks, below 3.5 ppm, bear some resemblance to the spectrum of 2-pyrrolidone,\(^{16}\) but others above 3.5 ppm do not. A similar resemblance is found for the N-vinyl-2-pyrrolidone monomer,\(^{17}\) which has an additional vinyl signature absent in Figure 3.

Dialysis was performed on the PVP-1 solution using a membrane with a 1 kD cutoff. The results are seen in Figure 4. It is the peaks above 3.5 ppm that are reduced, bringing the spectrum more in line with those of PVP-2 and the S-A sample. Clearly, a protracted loss of some species occurs on dialysis.

**DISCUSSION**

IR spectroscopy has shown little difference between PVP-1 and PVP-2, that difference being in the existence of a minor peak at ~1020 cm\(^{-1}\), while XPS shows that, on dissolution, PVP-1 shows the presence of a new amide species (N1sB and O1sB) in an environment different from that of the PVP polymer (N1sA and O1sA). The NMR spectrum of PVP-1 confirms that a particular chemical species is slowly removed on dialysis, bringing PVP-1 in line with both PVP-2 and the sample obtained from Sigma-Aldrich.

A consideration of the free radical polymerization process\(^2\) indicates that there are several possibilities that may fit our findings. As the first possibility, PVP-1 may not have undergone the final hydrolysis step that produces free 2-pyrrolidone, a water-soluble \(\gamma\)-lactam.\(^2\) That is, what we may have caused to occur to PVP-1 on aqueous dissolution was the final hydrolysis step, which produces an aldehyde chain termination and free 2-pyrrolidone. This appears to be the case, as revealed by the new N 1s and O 1s XPS peaks, indicating a new amide environment on aqueous hydrolysis. However, the noise common to all samples correlates directly with the NMR spectrum of 2-pyrrolidone (see Figure 5), suggesting some retention, in all cases, following the final hydrolysis step during manufacture. That is, in the case of PVP-1, some additional 2-pyrrolidone appears to be formed, accounting for the higher than expected end group concentrations in Table 1 (see note f).

As a second possibility, PVP is known to entrain the monomer, N-vinyl-2-pyrrolidone, during polymerization,\(^{18}\) which must later be removed. It may be that total monomer removal did not occur on manufacture. N-Vinyl-2-pyrrolidone is reported to yellow on aging,\(^{19,20}\) as does our PVP-1. However, as noted earlier, there is no vinyl signature in the 2-pyrrolidone spectrum, eliminating that possibility. The absence of N-vinyl-2-pyrrolidone monomer, but not of the 2-pyrrolidone starting material, is surprising, but is consistent in all our samples.

As a third possibility, thermal degradation was also considered. However, since N-vinyl-2-pyrrolidone is known to evolve on heating\(^21\) and there is no evidence for it, this possibility was also eliminated.
Table 1. XPS Peak Attributions

| peak  | attribution | PVP-1 powder | PVP-1 dissolved and dried | PVP-2 powder |
|-------|-------------|--------------|----------------------------|--------------|
|       |             | binding energy (eV) | at. % | binding energy (eV) | at. % | binding energy (eV) | atomic percent |
| C1sA  | CH₃<sup>a</sup> | 285          | 20.2 | 285          | 21.4 | 285          | 29.9          |
| C1sB  | CH₂<sup>a</sup> | 285.9        | 21.4 | 285.9        | 26.5 | 285.9        | 26.4          |
| C1sC  | C–O<sup>b</sup> | 287.1        | 14.5 | 286.8        | 13.2 | 286.6        | 5.6           |
| C1sD  | C=O         | 288.2        | 6.8  | 288.1        | 8.5  | 287.8        | 11.6          |
| N1sA  | C–N<sup>c</sup> | 399.7        | 7    | 399.6        | 3.5  | 399.8        | 12.2          |
| N1sB  | new C–N<sup>d</sup> | 400.5        | 1.1  | 400.3        | 5.7  |              |               |
| O1sA  | C=O<sup>e</sup> | 531.2        | 8.3  | 531.2        | 7.3  | 531.2        | 12.9          |
| O1sB  | new C=O<sup>d</sup> | <sup>c</sup> | <sup>c</sup> | <sup>c</sup> | 532.2 | 7.6           |
| O1sC  | C–OH        | 533.3        | 20.6 | 533.3        | 6.3  | 532.6        | 1.4           |

<sup>a</sup>Minimum number of peaks were used that represent all five of the CH₃ contributions, given our instrument resolution of 0.7 eV. C1sB contains the C–N contributions. <sup>b</sup>Mostly from the C–OH chain terminations. <sup>c</sup>From the PVP polymer termination. <sup>d</sup>From the free contaminant. The O1sB component of the PVP-1 powder was not obvious. <sup>e</sup>Not obvious prior to dissolution and drying. <sup>f</sup>A combination of terminal hydroxyl and aldehyde groups falling between them in binding energy. The theoretical values are 0.34% for each; the peaks are too small to separate with confidence.
We are thus left with the conclusion that PVP-1 was incompletely hydrolyzed during manufacture, with further hydrolysis continuing on aqueous dissolution. However, an additional possibility presents itself. Pharmacologically, PVP is an excipient (i.e., pharmacologically inactive). Despite this, there have been occasional reports of adverse reactions when using PVP (we do not refer here to PVP-iodine, which has its own adverse reactions). Our results suggest that these adverse reactions may, in fact, have been due to either or both of the following causes:

- Unhydrolyzed 2-pyrrolidone chain ends, which subsequently hydrolyze in the human body, introduce more than the trace amounts of 2-pyrrolidone normally found in PVP; Safety Data Sheets, furnished by all 2-pyrrolidone suppliers, invariably indicate that, if ingested, it should immediately be diluted by drinking copious amounts of water, and medical help should be sought.
- Hydroperoxide contaminants, formed during the H₂O₂-catalyzed polymerization of N-vinyl-2-pyrrolidone, as well as the PVP-H₂O₂ complex known to be formed are all cytotoxic due to their abilities to produce free radicals, which lead to the formation and propagation of reactive oxygen species (ROS) that are toxic. These problems and others, such as the ROS degradation of the drugs with which PVP is mixed for delivery, have been cited and cautioned against for over three

Table 2. NMR Peak Attributions

| location          | chemical shift (ppm) |
|-------------------|----------------------|
| CH₂ adjacent to N | 3.1–3.3              |
| CH₂ adjacent to C═O | 2–2.5               |
| CH₂ between       | 1.6–2                |
| CH chain          | 3.6–4                |
| CH₁ chain         | 1.8–2.5              |

*Reference 15.*
...decades. Concerning the spectral identification of hydroperoxides, there is a paucity of evidence available in the literature that points specifically to the O−O bond only one unique peak exists in the region above 1000 cm⁻¹ because of O−O stretching. The reader should recall our Fourier transform infrared spectroscopy (FTIR) results, cited earlier, in which a peak at 1020 cm⁻¹ was found for PVP-1 but for no other sample. We posit that this peak indicates the presence of excess hydroperoxide in PVP-1. While it may also be that certain individuals are allergically predisposed to PVP, this appears unlikely, given its heavy use in the pharmaceutical industry. Rather, the aforementioned adverse reactions may well be due to the contaminants we have cited: the 2-pyrrolidone, produced by an initially incomplete hydrolysis, and the ROS produced by peroxide and hydroperoxide contaminants. Concerning the presence of peroxides and hydroperoxides, PVP was “found to contain substantial concentrations of hydroperoxides with significant lot-to-lot and manufacturer-to-manufacturer variations.” Further, the action of free radicals produced by the ROS also contributes to the yellowing, embrittlement, and opacity of the aqueous PVP-1 solutions on drying, as mentioned earlier.

In clarifying the reason for the dilution stability of Ag NP dispersions made with PVP-1, a recent publication demonstrated that 2-pyrrolidone does, in fact, act as a ligand to Ag ions. The resultant structure is found in the Cambridge Crystallographic Data Centre as number 842454. Rotatable 3D models at the site show that 2-pyrrolidone is bonded to the Ag ion by a coordinate covalent bond using the lone pair on the carbonyl O; no alkoxide bond is formed. This is undoubtedly what also happens with PVP, explaining both the lack of substantial change in the amide I peak as well as the absence of an alkoxide peak on reaction with Ag NPs. The retention of dispersion stability on dilution, in the case of PVP-1, suggests the reasons to be (1) the excess 2-pyrrolidone present and (2) that the bond formed between Ag and 2-pyrrolidone is stronger that formed between Ag and PVP, the latter washing off more easily on dilution.

■ CONCLUSIONS

XPS and NMR have been used to identify contaminants in our samples of PVP, something the normally used FTIR spectroscopy was unable to do: FTIR spectroscopy was incapable of distinguishing between PVP-1 (incomplete final hydrolysis step) and PVP-2 (normal preparation) samples of PVP because the 2-pyrrolidone released in the final hydrolysis step of PVP-1 has an IR spectrum that differs little from that of PVP-2. Both XPS and NMR, which can differentiate between similar structures in different environments, are better choices. Of the two, NMR appears easier to adapt commercially. Both give evidence of the presence of contaminants, which are identified as 2-pyrrolidone and hydroperoxides.

■ MATERIALS AND METHODS

The samples used here were purchased from Chinese suppliers (not manufacturers). All were grade K30, which indicates an ostensibly highly pure, pharmaceutically acceptable, linear polymer having a molecular weight of ~40,000 g/mol. The supplier of PVP-1, which permitted the aqueous dilution of PVP-stabilized Ag NPs without losing stability, was unable to furnish a similar material on subsequent purchases: the samples of PVP subsequently purchased from this supplier functioned as did samples purchased from the other suppliers, with PVP-stabilized Ag NPs losing dispersion stability on aqueous dilution. IR spectra over the range of 400–4000 cm⁻¹ at a resolution of 4 cm⁻¹ were obtained using a Bruker Alpha IR spectrometer; 64 scans for the initial powders and 96 scans for the dried solutions were coadded to improve S/N. The initial powder samples were deposited onto a diamond plate; aqueous samples were dropped onto freshly cleaned silica and dried. Replicas run for all samples were identical.

XPS was carried out using a VG ESCALAB 3 MK II (Thermo VG Scientific) spectrometer. Non-monochromated Mg Kα X-rays (hv = 1253.6 eV) gave an instrument resolution of 0.7 eV. Initial powder samples placed on a Cu tape were compressed, thick enough (~1 mm) to assure no evidence of Cu in the scans. Aqueous samples were permitted to dry before insertion into the apparatus and further dried in the preparation chamber before insertion into the analysis chamber; the analysis chamber pressure was <10⁻⁹ Torr. High-resolution spectra were obtained at a perpendicular takeoff angle using a pass energy of 20 eV (step size: 0.05 eV; step dwell time: 200 ms). Following Shirley background removal, the component peaks were separated by VG Avantage software. The binding energy was calibrated by moving the C
1H NMR spectra were obtained on a Bruker AV400 spectrometer operating at 400 MHz. Samples were dissolved in D$_2$O (20 mg/mL), and 32 scans were coadded at 25 °C. Dialysis was carried out over a week using a membrane with a 1 kD cutoff. Replicas run for all samples were identical.

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**Notes**

The authors declare no competing financial interest.

**REFERENCES**

(1) http://www.polyvinylpyrrolidone.com.cn/news-2.html (accessed June 3, 2020).

(2) Haaf, F.; Sanner, A.; Straub, F. Polymers of N-Vinylpyrrolidone: Synthesis, Characterization and Uses. Polym. J. 1985, 17, 143–152.

(3) Koczkur, K. M.; Mouidakoudis, S.; Polavarapu, L.; Skrabalak, S. E. Polyvinylpyrrolidone (PVP) in nanoparticle synthesis. Dalton Trans. 2015, 44, 17883–17905.

(4) Song, Y.-J.; Wang, M.; Zhang, Y.-Y.; Wu, J.-Y.; Zhang, T. Investigation of the role of the molecular weight of polyvinylpyrrolidone in the shape control of high-yield silver nanospheres and nanowires. Nanoscale Res. Lett. 2014, 9, 17.

(5) Al-Saidi, W. A.; Feng, H.; Fichthorn, K. A. Adsorption of Polyvinylpyrrolidone on Ag Surfaces: Insight into a Structure-Directing Agent. Nano Lett. 2012, 12, 997–1001.

(6) Mullitt, P. S.; Susbo, N. M.; Reavaprasadu, N.; Karamanis, P.; Leszcynski, J. Surface enhanced Raman spectroscopy (SERS) and density functional theory (DFT) study for understanding the regioselective adsorption of pyrrolidinone on the surface of silver and gold colloids. J. Mol. Struct. 2009, 935, 32–38.

(7) Wang, H.; Qiao, X.; Chen, J.; Wang, X.; Ding, S. Mechanisms of PVP in the preparation of silver nanoparticles. Mater. Chem. Phys. 2005, 94, 449–453.

(8) Gao, Y.; Jiang, P.; Liu, D. F.; Yuan, H. J.; Yan, X. Q.; Zhou, Z. P.; Wang, J. X.; Song, L.; Liu, L. F.; Zhou, W. Y.; Wang, G.; Wang, C. Y.; Xie, S. S.; Zhang, J. M.; Shen, D. Y. Evidence for the Monolayer Assembly of Poly(vinylpyrrolidone) on the Surfaces of Silver Nanowires. J. Phys. Chem. B 2004, 108, 12877–12881.

(9) Bonet, F.; Tekaia-Elhissi, K.; Sarathy, K. V. Study of interaction of ethylene glycol/PVP phase on noble metal powders prepared by polyl process. Bull. Mater. Sci. 2000, 23, 165–168.

(10) Prokopenko, N. A.; Bethea, I. A.; Clemens, C. J., IV; Klimek, A.; Wargo, K.; Spivey, C.; Waziri, K.; Grushow, A. The effect of structure on hydrogen bonding: Hydrogen bonded lactam dimers in CCl$_4$. Phys. Chem. Chem. Phys. 2002, 4, 490–495.

(11) Zhang, Z.; Zhao, B.; Hu, L. PVP Protective Mechanism of Ultrafine Silver Powder Synthesized by Chemical Reduction Processes. J. Solid State Chem. 1996, 121, 105–110.

(12) Huang, H. H.; Ni, X. P.; Loy, G. L.; Chew, C. H.; Tan, K. L.; Loh, F. C.; Deng, J. F.; Xu, G. Q. Photochemical Formation of Silver Nanoparticles in Poly(N-vinylpyrrolidone). Langmuir 1996, 12, 909–912.

(13) Socrates, G. Infrared and Raman Characteristic Group Frequencies, 3rd ed.; Wiley: New York, 2001, p 143.

(14) https://srdata.nist.gov/XPS/ (accessed May 18, 2020).

(15) Loria-Bastarrachea, M. I.; Herrera-Kao, W.; Cauich-Rodríguez, J. V.; Cervantes-Uc, J. M.; Vázquez-Torres, H.; Ávila-Ortega, A. A TG/FTIR study of the thermal degradation of poly(vinyl pyrrolidone). J. Therm. Anal. Calorim. 2011, 104, 737–742.

(16) https://www.chemicalbook.com/spectrumen_616-45-5_1Hnmr.htm (accessed May 18, 2020).

(17) https://www.chemicalbook.com/SpectrumEN_88-12-0_1HNMR.htm (accessed May 18, 2020).

(18) Turner, D. T.; Schwartz, A. The glass transition temperature of poly(N-vinyl pyrrolidone) by differential scanning calorimetry. Polymer 1985, 26, 757–762.

(19) National Industrial Chemicals Notification and Assessment Scheme (Australia). Priority Existing Chemical Report No. 11, 1-Vinylpyrrolidone, February, 2000.

(20) https://en.wikipedia.org/wiki/N-Vinylpyrrolidone (accessed May 18, 2020).

(21) Loria-Bastarrachea, M. I.; Herrera-Kao, W.; Cauich-Rodríguez, J. V.; Cervantes-Uc, J. M.; Vázquez-Torres, H.; Ávila-Ortega, A. A TG/FTIR study on the thermal degradation of poly(vinyl pyrrolidone). J. Therm. Anal. Calorim. 2011, 104, 737–742.

(22) https://en.wikipedia.org/wiki/Polyvinylpyrrolidone (accessed May 18, 2020).

(23) Modhave, D.; Barrios, B.; Paudel, A. PVP–H$_2$O Complex as a New Stressor for the Accelerated Oxidation Study of Pharmaceutical Solids. Pharmaceut. Pharmacol. 2019, 11, 457.

(24) https://en.wikipedia.org/wiki/Reactive_oxygen_species (accessed May 21, 2020).

(25) Wasylaschuk, W. R.; Harmon, P. A.; Wagner, G.; Harman, A. B.; Templeton, A. C.; Xu, H.; Reed, R. A. Evaluation of hydroperoxides in common pharmaceutical excipients. J. Pharmaceut. Sci. 2007, 96, 106–116.

(26) Bühler, V. Kolidon polyvinylpyrrolidone Excipients for the Pharmaceutical Industry, 9th ed.; BASF SE: Ludwigshafen, Germany, 2008; Chapter 2.2.9.

(27) Wu, Y.; Levons, J.; Narang, A. S.; Raghavan, K.; Rao, V. M. Reactive Impurities in Excipients: Profiling, Identification and Mitigation of Drug-Excipient Incompatibility. AAPS PharmSciTech 2011, 12, 1248–1263.

(28) El Amri, N.; Roger, K. Polyvinylpyrrolidone (PVP) impurities drastically impact the outcome of nanoparticle syntheses. J. Colloid Interface Sci. 2020, 576, 435–443.

(29) Socrates, G. Infrared and Raman Characteristic Group Frequencies, 3rd ed.; Wiley: New York, 2001; p 105.
(30) Fritsch, J.; Schumm, B.; Biedermann, R.; Grothe, J.; Kaskel, S. A New Silver-Based Precursor as Ink for Soft Printing Techniques. *Eur. J. Inorg. Chem.* 2012, 2012, 878−883.

(31) https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=842454&DatabaseToSearch=Published (Accessed May 19, 2020).

(32) Maslowsky, E., Jr. Vibrational Spectra of Organometallic Compounds; Wiley-Interscience: New York, 1977; Chapter I.E.6.

(33) Adams, D. M. Metal–Ligand and Related Vibrations; St. Martin’s Press: New York, 1968; Chapter 5.6.