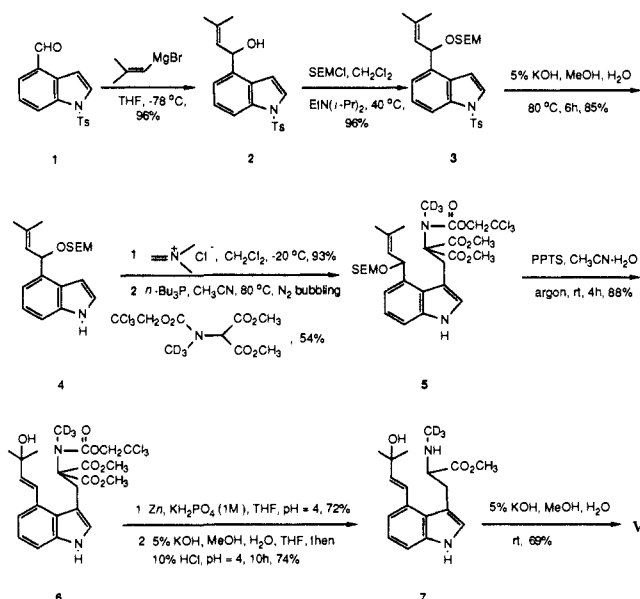


Scheme I. Synthesis of the Amino Acid V

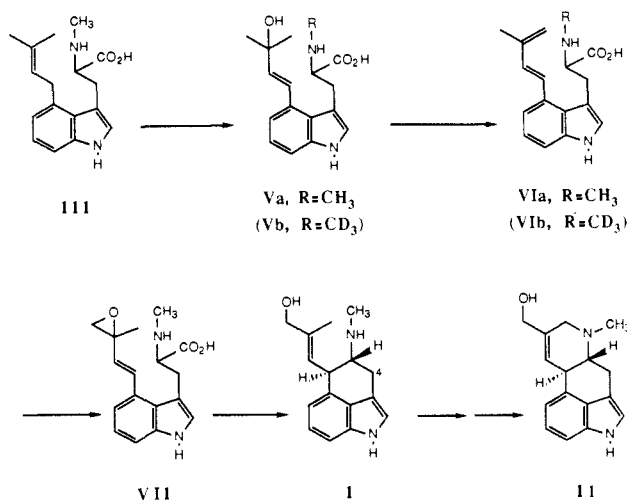


A sample of Vb (9 mg) was fed to a 50-mL replacement culture of *Claviceps sp.* strain SD58 as described earlier.^{6,7} After incubation at 25 °C with shaking for 2 days, II was isolated and subjected to GC-MS analysis.⁶ The mass spectrum showed the presence of only M and M + 3 species in the molecular ion of II, and their ratio corresponded to 33% specific incorporation of Vb into II. A repetition of the experiment with a separately synthesized sample (5 mg) gave 9% specific incorporation. The high and specific (no enhanced M + 1 or M + 2 species) incorporation of Vb into II leaves no doubt in the specific precursor role of this compound.

The present result would suggest that biosynthetically the tertiary alcohol is converted by dehydration to the diene VIA. This intermediate may then be epoxidized by cytochrome P-450 to the vinyl oxirane VII, which has been proposed⁸ to undergo decarboxylative ring closure via an S_N2' process to provide chanoclavine. Further support of this notion comes from trapping experiments with Vb. To a replacement culture containing unlabeled L-tryptophan (1 mg), D,L-mevalonic acid (2 mg), and L-methionine (1 mg) was added Vb (10 μ g). After 1 h incubation with shaking, V was reisolated by filtration and 1-butanol extraction of the filtrate, methylated with CH_2N_2 , and analyzed by GC-MS. An authentic sample of Vb methylated in the same way showed two peaks of t_{ret} 22.1 min and t_{ret} 21.7 min, identified by their mass spectra as the methyl esters of N-methyl Vb and VIb, respectively. The GC-MS of the reisolated V showed the same two peaks; the spectrum of the methyl ester of N-methyl Vb showed no dilution with Va, but the spectrum of the t_{ret} 21.7 min peak indicated dilution of the VIb with 19% VIA. Hence, while there is no evidence for the presence of Va in the culture, the presence of VIA is clearly indicated. This was confirmed by working up replacement cultures (2 \times 100 mL, 3 h) in the same way without any addition of V and demonstrating, by GC-MS with selective ion monitoring, the presence of VIA, as the methyl ester of its N-methyl derivative, in the methylated extract.

On the basis of these results we propose the reaction sequence shown in Scheme II for the closure of ring C in ergot alkaloid biosynthesis. Whether Va is a true intermediate in this sequence or whether the diene can be formed more directly from III must in light of the negative outcome of the trapping experiment remain open. Further efforts to examine the laboratory synthesis and

Scheme II. Proposed Reaction Sequence for C-Ring Formation in Ergot Alkaloid Biosynthesis



biosynthetic incorporation of the proposed diene and epoxide intermediates are underway.

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Supplementary Material Available: A listing of spectroscopic and analytical data for compounds 2-7 and Va (3 pages). Ordering information is given on any current masthead page.

Convenient Preparation and Structures of Selenometalates MoSe_4^{2-} , WSe_4^{2-} , and MoSe_9^{2-} from Polyselenide Anions and Metal Carbonyls

Samuel C. O'Neal and Joseph W. Kolis*

Department of Chemistry, Clemson University
Clemson, South Carolina 29634

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The tetrathiometalates, MoS_4^{2-} and WS_4^{2-} , and their tetrahedral analogues such as VS_4^{2-} have been well known for many years.^{1,2} They serve as building blocks for metalloenzyme models and can act as precursors and models for hydrodesulfurization catalysts.²⁻⁷ In contrast, the selenium analogues, though known, have received very little study.^{8,9} Recently, however, workers have begun exploring the chemistry of binary metal selenides with promising results.^{10,11}

We have been investigating the reactions of soluble polychalcogenides extracted from Zintl phases, with metal salts¹² and metal carbonyls.¹³ It was found that polytellurides react cleanly

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(7) The original procedure⁶ was modified to shake the resuspended mycelia for 2 h before the final filtration and suspension in the incubation buffer. This reduced considerably the amount of preformed II remaining in the cells.

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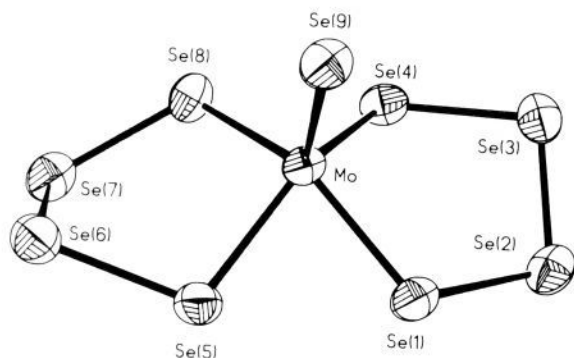


Figure 1. ORTEP view of the anion MoSe_9^{2-} . Some important distances, in Å are as follows: Mo–Se(1), 2.432 (4); Mo–Se(4), 2.505 (4); Mo–Se(5), 2.472 (4); Mo–Se(8), 2.481 (4); Mo–Se(9), 2.270 (4); Se(1)–Se(2), 2.461 (5); Se(2)–Se(3), 2.291 (5); Se(3)–Se(4), 2.384 (5); Se(5)–Se(6), 2.395 (5); Se(6)–Se(7), 2.307 (5); Se(7)–Se(8), 2.446 (5). Some important angles are as follows: Se(1)–Mo–Se(4), 91.9 (1); Se(5)–Mo–Se(8), 92.9 (1); Se(1)–Mo–Se(5), 76.9 (1); Se(4)–Se(8), 74.0 (1); Se(1)–Mo–Se(9), 107.3 (1); Se(4)–Mo–Se(9), 110.5 (2); Se(5)–Mo–Se(9), 108

with group 6 metal carbonyls to form metal polytelluride chelates $(\text{CO})_4\text{MTe}_4^{2-}$.¹³ However, when this reaction was extended to the polyselenides, we were surprised to find that instead of metal carbonyl fragments with chelating selenium rings, the metal tetraselenides MoSe_4^{2-} and WSe_4^{2-} were isolated in high yield. This unexpected result represents a far more convenient preparation of these molecules than previous methods and paves the way for reactivity and spectroscopic studies. In this communication we report the preparation of these two important molecules as well as the synthesis and structure of MoSe_9^{2-} . This is the first soluble binary molybdenum polyselenide except for the parent MoSe_4^{2-} .

The tetraselenometalates were isolated as their tetraphenylphosphonium salts from the reaction of K_2Se_3 ¹⁴ and $\text{M}(\text{CO})_6$ in DMF. A reasonable balanced equation is



Equal amounts of K_2Se_3 and $\text{M}(\text{CO})_6$ were dissolved in dimethylformamide (DMF), and the solution was heated to 90 °C for 1 h, 2 equiv of $(\text{C}_6\text{H}_5)_4\text{PBr}$ were added, and the solution was filtered. An equal volume of THF was added, and, after storage at 4 °C overnight, the product was isolated in 60% yield as well formed crystals of composition $[(\text{C}_6\text{H}_5)_4\text{P}]_2[\text{MSe}_4]$,¹⁵ with the molybdenum compound being bright blue and the tungsten analogue being cherry red, as previously reported.¹

Both compounds were characterized by single-crystal X-ray structural analysis.¹⁶ The structure of the tungsten compound has been reported both as the ammonium¹⁷ and cesium¹ salt. To

our knowledge, the structure of the molybdenum compound has not been determined. Neither compound is structurally remarkable, as both contain tetrahedrally coordinated metal selenide with well-separated counterions. The bond lengths of the tungsten compound are similar to those reported previously (2.314 (1) Å), while those of the molybdenum complex are slightly shorter (2.293 (1) Å).

When MoSe_4^{2-} is combined with 5 equiv of grey selenium at room temperature in DMF solution, it reacts smoothly and completely in 2 h to form MoSe_9^{2-} in high (65%) yield. Again, slow addition of an equal amount of THF results in deep red crystals of $[(\text{C}_6\text{H}_5)_4\text{P}]_2[\text{MoSe}_9]$, suitable for X-ray diffraction study.¹⁸ The structure is similar to that of the sulfur analogue, MoS_9^{2-} .¹⁹ It contains two four-membered selenium rings chelated to a Mo(IV) center along with a terminal selenide, with the coordination geometry around the metal center being square pyramidal (see Figure 1). The tetraselenium rings are puckered and show a variation in Se–Se bond lengths from 2.307 (5) to 2.461 (5) Å. This variation is similar to those observed previously in sulfur rings and has been attributed to π bonding between the sulfur and the metal atom, resulting in weakening of the adjacent S–S bonds.²⁰ Crystallographically characterized terminal molybdenum selenides are rare, but the bond distance in this molecule is quite short (2.270 (4) Å). This is shorter than the Mo=Se distance in both MoSe_4^{2-} (2.293 (1) Å) as well as in the linear $[(\text{HB}(\text{pz})_3)\text{Mo}(\text{CO})_2]\text{Se}$ (2.323 (1) Å).²¹

It is well known that solutions of metal polychalcogenides are complex equilibria of a variety of species. Thus, the nature of the compound isolated depends on solvent, counterion, and conditions. When MoSe_4^{2-} is combined with elemental sulfur, MoS_9^{2-} can be isolated only in the presence of Et_4N^+ salts. In the presence of Ph_4P^+ , a mixture of $\text{Mo}_2\text{S}_{10}^{2-}$ and $\text{Mo}_2\text{S}_{12}^{2-}$ is isolated.¹⁹ Similarly, when WSe_4^{2-} is reacted with elemental selenium, a mixture of $\text{W}_2\text{Se}_{10}^{2-}$ isomers is obtained.^{10a} However in our case, MoSe_9^{2-} seems to be the major product and can be isolated in good yield. The contrast in behavior of the tungsten selenides versus the molybdenum selenides is probably due to the ease of reduction of the formal Mo(VI) state versus the W(VI) state, as has been discussed previously.²²

The reaction to form the tetraselenometalates from the metal carbonyls is unexpected, and the mechanism of formation is unknown. Formally, the reaction involves an oxidation of the metal center from 0 to 6+. Presumably, Se_3^{2-} is acting as the oxidizing agent. It is known that H_2O_2 will oxidatively decarbonylate metal carbonyls and form oxo complexes,²³ but it seems a bit more unusual for a soft dianion to oxidize a metal to its maximum oxidation state. Although heating to 90 °C causes the reaction to proceed more quickly, it is not necessary. The tetraselenides will form equally well after stirring at room temperature for several days. We have preliminary evidence that the reaction may proceed via a chelating polyselenide ring (analogous to the polytellurides) possibly followed by conversion to a diselenocarbonate intermediate.²⁴ These ideas will be discussed more fully in a later paper, and further mechanistic speculation is inappropriate at this time.

(18) Anal. Calcd for $\text{C}_{48}\text{H}_{40}\text{P}_2\text{MoSe}_9$: C, 38.79; H, 2.69. Found: C, 38.62; H, 2.78. Crystal data for $[(\text{C}_6\text{H}_5)_4\text{P}]_2[\text{MoSe}_9]$: triclinic, $P\bar{1}$, $Z = 2$, $d = 1.97$, $\mu = 68.45 \text{ cm}^{-1}$, $a = 10.013$ (8) Å, $b = 12.595$ (9) Å, $c = 20.597$ (23) Å, $\alpha = 106.30$ (7)°, $\beta = 92.35$ (8)°, $\gamma = 96.72$ (6)°, $V = 2497.8$ (39) Å³, $T = 24$ °C, 6975 reflections read to 2θ (Mo $K\alpha$) = 45° with $R = 0.0715$ for 3206 reflections of $F_o^2 > 3\sigma(F_o^2)$.

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(14) K_2Se_3 was prepared by combining the elements in the proper stoichiometry in a flask containing a glass stir bar and a Teflon valve. Dry ammonia was distilled onto the elements, and the flask was closed off. The flask was immersed in a slush bath at –78 °C and stirred for 2 h. The liquid ammonia was removed from the dark green solution leaving a dry gray microcrystalline powder which could be stored under an inert atmosphere indefinitely.

(15) Anal. Calcd for $\text{C}_{48}\text{H}_{40}\text{MoP}_2\text{Se}_4$: C, 52.81; H, 3.69; Se, 28.99. Found: C, 51.17; H, 3.79; Se, 27.43. Anal. Calcd for $\text{C}_{48}\text{H}_{40}\text{P}_2\text{Se}_4\text{W}$: C, 48.32; H, 3.42; Se, 26.81. Found: C, 45.32; H, 3.37; Se, 26.11. Note: We consistently obtained results which were slightly low for all elements, even in highly crystalline samples. We attribute this to trace amounts of KBr co-crystallizing with the sample.

(16) Crystal data for $[(\text{C}_6\text{H}_5)_4\text{P}]_2[\text{MoSe}_4]$: monoclinic, $C2/c$, $Z = 4$, $d = 1.62$, $\mu = 36.10 \text{ cm}^{-1}$, $a = 11.191$ (6) Å, $b = 19.648$ (7) Å, $c = 20.352$ (7) Å, $\beta = 91.20$ (4)°, $V = 4474.0$ (24) Å³, $T = 24$ °C, 6235 reflections read to 2θ (Mo $K\alpha$) = 45° with $R = 0.0395$ for 1826 unique reflections of $F_o^2 > 3\sigma(F_o^2)$. Crystal data for $[(\text{C}_6\text{H}_5)_4\text{P}]_2[\text{WSe}_4]$: monoclinic, $C2/c$, $Z = 4$, $d = 1.78$, $\mu = 60.52 \text{ cm}^{-1}$, $a = 11.261$ (4) Å, $b = 19.715$ (6) Å, $c = 20.416$ (7) Å, $\beta = 91.77$ (3)°, $V = 4403.3$ (26) Å³, $T = 24$ °C, 6519 reflections read to 2θ (Mo $K\alpha$) = 45° with $R = 0.0330$ for 2029 unique reflections of $F_o^2 > 3\sigma(F_o^2)$.

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However, the reaction is synthetically useful in that it provides a convenient high yield route to the tetraselenometalates and their derivatives.

Acknowledgment. We acknowledge the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work. We are grateful to Jim Ibers for preliminary communication of results.

Supplementary Material Available: Tables of atomic coordinates, bond distances and angles of all atoms, anisotropic thermal parameters, and H atom coordinates for $[(C_6H_5)_4P]_2[MoSe_4]$, $[(C_6H_5)_4P]_2[WSe_4]$, and $[(C_6H_5)_4P]_2[MoSe_9]$ (3 pages); listing of calculated and observed structure factors (8 pages). Ordering information is given on any current masthead page.

Intramolecular Exchange Effects in Multiple Quantum Spectroscopy

Mark Rance

Department of Molecular Biology
Research Institute of Scripps Clinic
10666 North Torrey Pines Road
La Jolla, California 92037

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The effects of exchange processes in high resolution NMR spectroscopy have been investigated extensively, from both a theoretical and an experimental standpoint.¹ The sensitivity of NMR spectroscopy to exchange effects has provided a very powerful means to elucidate the exchange pathways and measure the rates for various types of chemical reorganization processes; NMR techniques which have been employed include line shape analysis,² double resonance methods such as saturation transfer,³ pulse experiments such as spin echo studies,⁴ and two-dimensional exchange spectroscopy.⁵ In the present communication, we would like to take a different perspective and demonstrate a possibility for recovering spectral information which is often lost due to exchange effects; this method is based on the insensitivity of certain multiple quantum coherences to some intramolecular exchange processes.

To illustrate this unique and potentially very useful feature of multiple quantum NMR spectroscopy,^{6,7} consider as a simple example a linear AMX spin system (J_{AX} coupling is not resolved) in which the A and X spins are undergoing mutual exchange. It is well known that if two spins are exchanging sites, their individual resonances will first broaden and then coalesce into an exchange-narrowed, single peak as the exchange rate k increases from slow to fast relative to the frequency separation of the unperturbed resonances, $\Delta\nu$. Due to substantial line-broadening, it is sometimes difficult to detect the NMR signal from exchanging spins when $k \sim \Delta\nu$; this is particularly true in many types of coherence transfer experiments where the resonances have antiphase multiplets and are thus severely attenuated due to self-

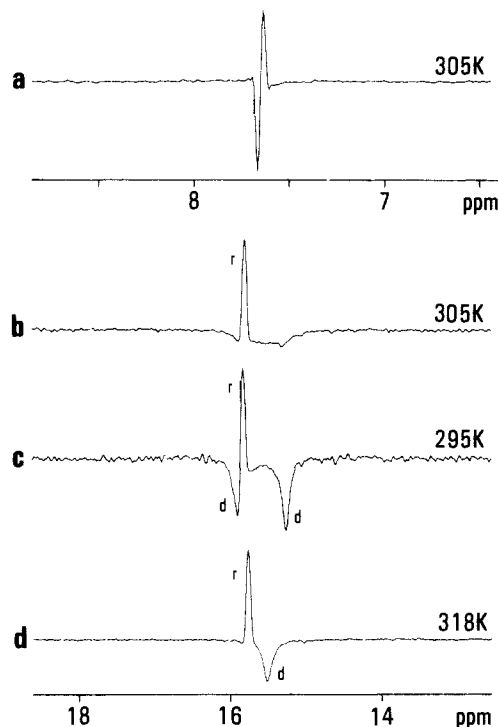


Figure 1. Slices taken from 2D 1H NMR spectra at the ω_2 chemical shift of the aromatic 4-H of Phe-45 in BPTI (in 2H_2O , 15 mM, pH 4.6) for (a) a double quantum-filtered COSY experiment and (b)–(d) double quantum experiments, at the temperatures indicated. In the DQF-COSY spectrum only a diagonal peak is detected, providing no information concerning the 3,5-H resonance frequencies. In the 2Q spectra the remote and direct peaks are labeled 'r' and 'd', respectively. (A ppm scale is the most convenient for interpreting the multiple quantum spectra, but note that it is not a chemical shift scale; the origin of this scale is such that $\omega_1 = 0$ Hz corresponds in ppm to twice the chemical shift of the transmitter frequency in the ω_2 dimension.) For each of the 2Q spectra shown, two adjacent slices from the 2D maps have been co-added because in the ω_2 dimension the direct and remote peaks have opposite phase characteristics¹⁵ (absorption/dispersion) and different multiplet component intensities so that the maxima occur at slightly different ω_2 frequencies. Note also that a multiple quantum excitation period of 30 ms was chosen, which is about optimum for the direct peaks but results in the remote peak having approximately half its maximum intensity. All experiments were run at 500 MHz on a Bruker AM500 spectrometer. The standard pulse sequence was used for the DQF-COSY experiment,^{9,12} while the conventional sequence for 2Q experiments⁷ (with 90° 'read' pulse) was modified by employing $(385_x^\circ - 325_x^\circ - 25_x^\circ)$ composite 90° pulses¹⁶ and EXORCYCLE phase-cycling¹⁷ of the 180° refocusing pulse to eliminate ω_1 phase errors arising from off-resonance effects.

cancelation when the line width is large compared to the active scalar coupling. In a 2D correlation experiment for instance, such as COSY⁸ or double quantum-filtered (DQF) COSY,⁹ the cross peaks expected for an AMX system will be extremely weak in the case where spins A and X are mutually exchanging at an intermediate rate. It is in this situation that multiple quantum spectroscopy has a unique advantage. As discussed by Braunschweiler et al.,⁷ it is possible to excite a so-called "remote" double quantum coherence between spins A and X in a linear AMX system through their mutual scalar coupling to spin M. The frequency of this 2Q transition is the sum of the single quantum frequencies of the A and X spins, which is independent of the mutual exchange of these spins. This AX 2Q coherence, unaffected by the $A \leftrightarrow X$ exchange process, can subsequently be transferred back to single quantum transitions of the M spin (which also are not exchange-broadened). As a result, in a 2D double quantum spectrum a remote peak at $\omega_1 = \Omega_A + \Omega_X$ and

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