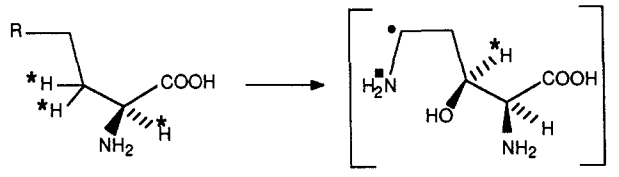
a spin-coupled doublet (J_{CN} = 2.7 Hz) for C-5 (152.6 and 154.7 ppm, respectively) with the lower field satellite superimposed on the natural-abundance singlet (1.4-Hz upfield isotope shift). Thus, both isotopes were retained and ornithine was demonstrated to be the primary precursor to both metabolites. This represents surprising apparent lack of metabolic economy since C-5 must subsequently be reoxidized to the amide oxidation state.

The subsequent metabolism of **3** has been probed with DL-[2,3,3-$^2H_3$]ornithine (**3b**),[23] this precursor having been prepared by exchange of **3** with D_2O in the presence of pyridoxal.[24] This feeding experiment afforded 3.6 mg of **1b** and 27 mg of **2b**. The

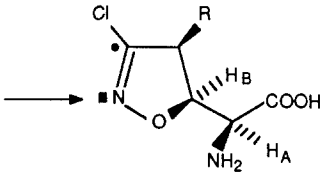


3, R=CH_2NH_2 **3a**, R=$^{13}CH_2^{15}NH_2$

4, R=COOH **3b**, R=CH_2NH_2, *H=^2H

5, R=$CONH_2$

6



1a, R=H, •=^{13}C, ■=^{15}N

2a, R=OH, " "

1b, R=H, H_A=H, H_B=^2H

2b, R=OH, " "

61.4-MHz ^2H NMR spectrum of **2b**[25] (27693 scans)[26] showed resonances for residual HOD (δ 4.93), for *tert*-butyl alcohol added as a chemical shift and deuterium quantitation reference (δ 1.27), and for deuterium at C-3 (δ 5.19).[27] Absolutely no deuterium was detectable at C-2, even though the signal to noise ratio would have allowed detection of 2% retention relative to C-3.

It is noteworthy that a complete loss of deuterium had also been obtained during incorporation of a variety of arginines labeled with deuterium at C-2 in the biosynthesis of streptothricin F,[8,28] for which we have postulated the involvement of β-hydroxyarginine, and in both cases we believe that the loss of this hydrogen may be mechanism-based and related to the hydroxylation. These results are in contrast to our finding of only a 70-80% loss of deuterium from C-2 of labeled arginines that were fed to *S. griseochromogenes* and ultimately incorporated into blasticidin S[10] via a 2,3-aminomutase reaction; in this case the partial loss was probably coincidentally due to an arginine racemase activity[29] unrelated to the blasticidin biosynthesis. The further metabolism of **3**, including the potential involvement of β-hydroxyornithine **6**, is currently under study. Townsend and Ho[30] recently reported strong evidence for ornithine as the direct primary precursor to the C_5 unit of clavulanic acid; since C-3 of ornithine is eventually oxygenated in this pathway, **6** may also be involved in this somewhat more cryptic metabolism.

Acknowledgment. Dr. David Martin and Shirley Gerpheide of the Upjohn Co. are thanked for providing samples of acivicin and 4-hydroxyacivicin, slants of *S. sviceus*, and the design of the baffled flask. The work was supported by grants from the Public Health Service (GM 32110) and the Oregon State University Environmental Health Sciences Center (NIESH Grant ES 00210) to S.J.G. NMR spectra were obtained on a Bruker AM 400 spectrometer purchased in part by grants from the National Science Foundation (CHE-8216190) and from the M. J. Murdock Charitable Trust to Oregon State University.

(20) Sweep width, 25 000 Hz; acquisition time, 1.3 s; 64 K data points; chemical shifts referenced to CH_3CN (1.3 ppm).

(21) ^{13}C NMR of **1**: 170.2 (C-1), 152.6 (C-5), 80.7 (C-3), 56.4 (C-2), 40.2 ppm (C-4).

(22) ^{13}C NMR of **2**: 170.4 (C-1), 154.7 (C-5), 81.7 (C-3), 77.2 (C-4), 53.1 ppm (C-2).

(23) DL-[2,3,3-$^2H_3$]Ornithine (**3**), 88.9 mg, mixed with 12.0 μCi of DL-[5-^{14}C]ornithine was fed in equal portions to ten 200-mL production broths at 48 h.

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(25) ^1H NMR of **1**: δ 3.4 (m, 2 H), 4.0 (d, 1 H, *J* = 3.2 Hz), 5.2 (1 H, m). ^1H NMR of **2**: δ 5.2 (dd, 1 H, *J* = 3.7, 4.4 Hz), 5.3 (d, 1 H, *J* = 8.5 Hz), 4.4 (d, 1 H, *J* = 4.1 Hz).

(26) Sweep width, 586.2 Hz; acquisition time 1.7 s; no. of scans 27 693; 2K data points zero filled to 8K; 2.0-Hz line broadening.

(27) The ^2H NMR spectrum of **1b** similarly showed retention of deuterium only at C-3 although, due to the small amount of sample, the signal to noise was much poorer.

(28) We have recently synthesized [2,3,3,5,5-$^2H_5$]arginine. The ^2H NMR spectrum of streptothricin F biosynthetically derived from this showed resonances due only to the labels at C-5: Wityak, J.; Gould, S. J., unpublished results.

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Aryl-Substituted Molecular Metal Oxide Clusters

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Incorporation of transition metals into and onto metal oxide aggregates has received increasing attention owing to the analogies being developed between such molecular clusters and extended phase, bulk oxide surfaces.[1-4] Organic molecules are known to undergo chemical reactions on oxide surfaces and so metal oxide clusters bearing purely organic substituents offer the prospect of obtaining further insight into this chemistry. Few examples exist of hydrocarbyl-substituted oxymetalates. These include $CH_2Mo_4O_{15}H^{3-}$, obtained from formaldehyde and $Mo_2O_7^{2-}$, in which a CH_2 unit bridges two Mo-O-Mo units,[5] heteroatom-substituted clusters of the types $R_2P_2M_5O_{21}^{4-}$ (M = Mo, W),[6,7] $R_2As_2Mo_6O_{24}^{4-}$,[8] and $(CH_3O)_4Mo_8O_{24}^{4-}$, which contains two bridging and two terminal methoxy groups.[9-11] Pyrolysis of $(R_3O)_3PW_{12}O_{40}$ produces the trialkyl derivatives $R_3PW_{12}O_{40}$ (R = CH_3, C_2H_5) which, at higher temperatures, form $H_3PW_{12}O_{40}$.[12] As a further elaboration of our solid-state syntheses of derivatives of molecular metal oxide clusters,[13] we report here a *general* route to neutral, aryl-substituted heteropolyanions of the type $(aryl)_{8-n}XM_{12}O_{40}$ (X = P, Si; M = Mo, W; *n* is the formal oxidation state of heteroatom X).

Metathetical reaction of aryl diazonium salts with Keggin ions provides $(arylN_2)_{8-n}XM_{12}O_{40}$ which, when pyrolyzed, forms

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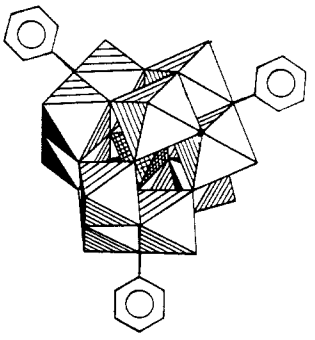

Figure 1. Proposed structure of $Ph_4SiW_{12}O_{40}$. The central SiO_4 unit is cross-hatched. One of the phenyl rings lies behind the plane of the paper.

$(aryl)_{8-n}XM_{12}O_{40}$. For example, addition of hydrated $(H_3O)_4SiW_{12}O_{40}$ to an acetonitrile solution of $PhN_2^+PF_6^-$ yields white, insoluble crystalline $(PhN_2)_4SiW_{12}O_{40}$ (**1**: IR $\nu_{N=N}$ 2269 cm^{-1}; ^{13}C CPMAS NMR 114 (C_{ipso}), 134 ($C_{meta\ and\ ortho}$), 143, 147 (C_{para}) ppm. On heating at 75 °C under vacuum, **1** undergoes rapid, quantitative loss of nitrogen to provide tan $Ph_4SiW_{12}O_{40}$ (**2**).[14] This synthetic method has broad general applicability and has been extended to a wide variety of aryldiazonium salts, readily obtainable from the corresponding anilines, and other molecular metal oxide clusters such as $SiMo_{12}O_{40}^{4-}$, $PW_{12}O_{40}^{3-}$, and $PMo_{12}O_{40}^{3-}$.

Aryldiazonium Keggin ion salts bearing electron-withdrawing ring substituents have significantly higher thermal stability but can be decomposed photochemically. Thus, for example, $(p\text{-}CH_3OPhNHPhN_2)_3PW_{12}O_{40}$ (**3**) undergoes nitrogen loss at 138 °C. Irradiation into the broad absorption band centered at 450 nm results in elimination of nitrogen and formation of $(p\text{-}CH_3OPhNHph)_3PW_{12}O_{40}$ (**4**). The photochemical syntheses are not quantitative, however, because of self-absorption of incident radiation.

The Keggin ion $PMo_{12}O_{40}^{3-}$ undergoes monoalkylation by $(CH_3)_3O^+BF_4^-$ and the X-ray structure of $CH_3PMo_{12}O_{40}^{2-}$ disclosed that the methyl group is attached to an oxygen atom which bridges two edge-shared molybdenum octahedra.[15] This compound provides a structural paradigm for $(aryl)_{8-n}XM_{12}O_{40}$, and we consider that the aryl substituents are similarly attached to bridging oxygen atoms in the cluster. The ^{13}C CPMAS NMR spectrum of **2** demonstrates peaks at 166 (C_{ipso}), 133 (C_{meta} and C_{para}), and 122 (C_{ortho}) ppm relative to $(CH_3)_4Si$. These chemical shift values are typical of oxygen-substituted aryl compounds such as anisole for which the corresponding shifts are 159.9, 129.5, 120.7, and 114.1 ppm[16] and furnish evidence that the aryl groups are in fact covalently bonded to the $SiW_{12}O_{40}$ cage, cf. Figure 1. Consistent with this is the observation that the infrared spectra of **1** and **2** in the W–O stretching region are essentially the same which argues against a W=O bonding site.

Compound **2** and its analogues are poorly soluble in nonreactive organic solvents. Typical of inorganic esters, it reacts with aqueous acetonitrile to form phenol, in 97% yield, and $SiW_{12}O_{40}^{4-}$. A search for anionic, partially hydrolyzed clusters has not been successful. We consider that the hydrolysis involves nucleophilic attack by hydroxide ion with cleavage of W–O bonds for, when this reaction is carried out with $H_2{}^{18}O$, the phenol does not incorporate the ^{18}O label. Remarkably, the hydrolysis also produces a ca. 3% yield of hydroxybiphenyls which also do not contain ^{18}O. The ortho/meta/para isomer ratio is 1:0.24:0.31 which is strongly suggestive of a free radical coupling process.[17] When **2** and $(p\text{-tolyl})_4SiO_{12}O_{40}$ are cohydrolyzed, cross-coupling products, viz., methylhydroxybiphenyls, are not detected. Similarly, they are not formed when *p*-cresol is added to the hydrolysis mixture. This indicates that the aryl groups which combine to give hydroxybiphenyl are confined to a region close to the surface of the $SiW_{12}O_{40}$ cluster and are not freely diffusing in solution.

We are continuing to investigate the chemistry of these and related hydrocarbyl oxymetalates in an effort to better understand the reaction mechanisms of the pendant aryl groups.

Acknowledgment. We are grateful to W. T. Conway, 3M Analytical and Properties Research Laboratory, for the thermogravimetric analyses.

(14) **1**: Anal. Calcd C, 8.7; H, 0.6; N, 3.4. Found C, 8.7; H, 0.6, N, 3.4. **2**: Anal. Calcd C, 9.0; H, 0.6; N, 0.0; found: C, 8.9; H, 0.7; N <0.1. Temperatures required for thermal elimination of N_2 from **1** and further quantitation of N_2 loss was achieved by thermogravimetric analysis.
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Synthesis of a 1,3-Bridged β-Lactam: A Novel, Anti-Bredt β-Lactam

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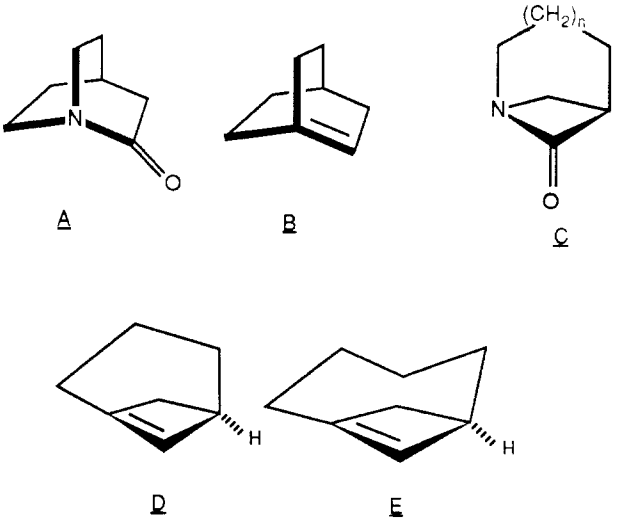
The β-lactam antibiotics have figured prominently in chemistry due to their desirable medicinal properties as chemotherapeutic agents, their structural novelty, and their attendant rich chemistry.[1] In the past few years, a plethora of structurally novel β-lactam antibiotics have been discovered from natural sources as well as the laboratories of academic and industrial scientists. In conjunction with an ongoing project in our laboratories, we desired the preparation of bicyclic amides containing the amide nitrogen in a bridgehead disposition. Hall[2] and others[3] have employed Bredt's rule, later modified by Wiseman,[4] Kobrich,[5] and Schleyer,[6] as a guide for predicting the stability and attendant isolability of N-bridgehead amides. However, due to the capacity of the nitrogen atom to assume a tetrahedral geometry, several "anti-Bredt amides" have been synthesized[7] such as 1-aza-bicyclo-[2.2.2]octan-2-one (A): the corresponding olefin B is predicted



to be an unstable olefin[8] with an olefin strain energy (OS)[6] of >40

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