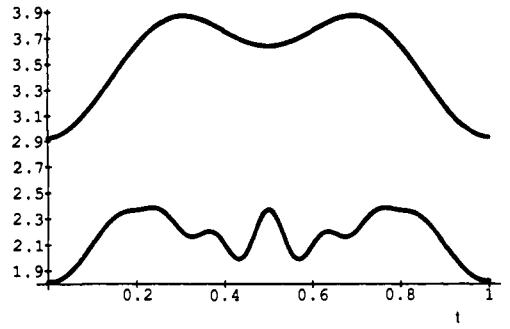

Figure 3. Valence sums for Hg as a function of the four-dimensional coordinate t. Top curve: for the average structure. Bottom curve: for the true structure including the modulation.

mercury atom as a function of the coordinate t. Figure 3 shows the results for both the average and the modulated structures. The Hg valence, which varies between 3.87 and 2.92 in the *average* structure, has, in the actual structure, much more reasonable values varying between 2.38 and 1.81, with a mean of 2.18. Thus the mercury atom has an average valency of close to 2, as may be expected, and a much smaller variation between unit cells than would have been the case in the absence of the modulation.

We conclude that the modulation in (BEDT-TTF)$Hg_{0.776}(SCN)_2$ is due to the coordination requirements of the central metal atom. The chemical nature of the modulation may be compared with modulations due to the lowering of the electronic energy in a valence band, such as occur in Peierls type metal–insulator transitions in low-dimensional solids. The continuous variation of the coordination, illustrated in Figure 1b, is highly unusual, but may become more common as additional complex solids are being synthesized.

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Enantioselective Synthesis of Mannostatin A: A New Glycoprotein Processing Inhibitor

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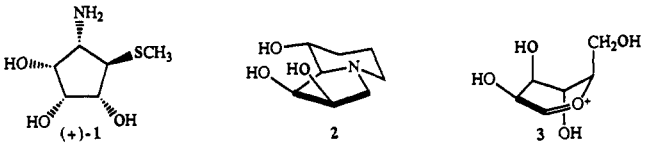
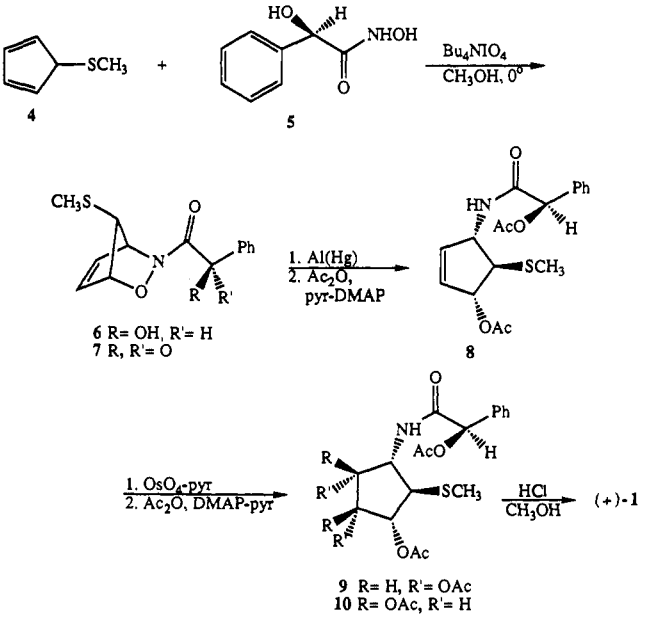
The emergence of N-linked oligosaccharides on glycoproteins as important structural and functional domains in carbohydrate–protein interactions (e.g., recognition,[1] adhesion,[2] and transport[3]) is in large part due to the development of glycosidase inhibitors which have helped unravel the detailed trimming and processing events following glycosylation.[4] Until recently these naturally occurring inhibitors of glycoside hydrolysis were polyhydroxylated monocyclic[5,6] or bicyclic[7,8] alkaloids resembling either

Scheme I



Scheme II



D-glucose or D-mannose.[9] However, in 1989 extracts of the soil microorganism *Streptoverticillium verticillus* were found to contain an unusual pentasubstituted cyclopentane **1** (Scheme I), which was named mannostatin A for its potent effect on rat epididymal α-mannosidase.[10] The structure and absolute stereochemistry of **1** shown in Scheme I were determined by X-ray diffraction.

Although its structure is quite different from the structures of known alkaloid-based inhibitors, compound **1** blocked Golgi processing mannosidase II more effectively than swainsonine (**2**) (IC_{50} = 200 nM;[8a] for **1**, 10–15 nM).[11] Such potent activity is all the more intriguing since mannostatin A bears little resemblance either to D-mannose or to the mannopyranosyl cation **3**, a putative hydrolysis intermediate.[12] Here we report a short, enantioselective total synthesis of **1** involving an unusual, syn-selective osmylation. Besides resolving certain questions surrounding the structure of **1**,[13] our work lays the groundwork for additional structure–activity studies of this remarkably potent new class of competitive glycosidase inhibitors.

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We reasoned that three of the five chiral centers in **1** might be fixed enantioselectively by asymmetric cycloaddition of the known 1-(methylthio)cyclopenta-2,4-diene[14] (**4**) with an appropriate chiral acyl-nitroso compound (Scheme II).[15] Subsequent osmylation of the bicyclic adduct **6** from the less hindered endo face would complete mannostatin's oxygenation pattern.

In the event, CH_3SCl (0.8 equiv) was stirred with a suspension of thallous cyclopentadienide (CCl_4, room temperature), and after the precipitated salts were filtered, crude **4** was combined with (*R*)-mandelohydroxamic acid (**5**) in the presence of Bu_4NIO_4 (0 °C, CH_3OH, 1 h) to afford a 2.6:1 ratio of adducts (30–35% overall from CH_3SCl). Flash chromatography and recrystallization gave the major diastereomer (mp 89–90 °C), which was assigned structure **6** on the basis of steric control of addition to the internally H-bonded acyl-nitroso compound.[16]

Vicinal hydroxylation of the bicyclic adduct proved more difficult than expected. For example, attempted catalytic osmylation using *N*-methylmorpholine *N*-oxide[17] formed the corresponding sulfoxides and sulfones of **6**,[18] whereas stoichiometric amounts of OsO_4 produced α-keto amide **7**. Therefore **6** was reduced (Al-Hg, THF-H_2O) and acetylated to furnish **8** (41% yield from **6**).[19]

Completion of the synthesis relied on a remarkable syn-directive effect which has recently been noted in the osmylation of such bis-allylically substituted cyclopentenes.[20] Although solvent and chelation effects have been invoked, no clear mechanistic explanation has emerged to account for such unusual stereoselectivity.[21] In fact stoichiometric osmylation of **8** in pyridine (1.5 equiv of OsO_4, room temperature, 20 h, 74%) occurred with exceptionally high facial selectivity. Acetylation of the initial diol mixture (resulting from solvent-promoted acetyl migration) produced a 20:1 ratio of tetraacetates **9** and **10** easily separable by chromatography. Hydrolysis of **9** (HCl-CH_3OH, 60 °C, 65% yield) afforded optically active mannostatin A hydrochloride, (+)-**1**·HCl, whose physical[22] and biological[23] properties were identical in every respect with those of an authentic sample.

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Supplementary Material Available: Full experimental details, including spectral and physical data, for the synthesis of **1** (3 pages). Ordering information is given an any current masthead page.

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(22) For synthetic **1**·HCl: $[\alpha]_D = +4.5°$ ($c = 0.24$, CH_3OH). For naturally occurring **1**·HCl: $[\alpha]_D = +5.9°$ ($c = 1.08$, CH_3OH). Note: All ^1H NMR data reported for **1** in ref 10b refer to an acid salt and not the free base. Published data include a systematic error of 0.61 ppm due to use of an external standard. We thank Professor A. D. Elbein for an authentic sample of mannostatin A.

(23) Synthetic (+)-**1** exhibited the same inhibitory activity as naturally occurring mannostatin A against Golgi processing mannosidase II. Moreover, a synthetic sample of (±)-**1**, prepared as in Scheme II from racemic **5**, possessed one-half the potency of (+)-**1**, indicating that the unnatural enantiomer is devoid of activity. We are grateful to Professor A. D. Elbein for conducting these assays.

Competitive Carbonylation Pathways from a Dialkyl A-Frame Complex

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In the carbonylation of transition-metal alkyl complexes, different reaction pathways leading to the formation of aldehydes and ketones have been described.[1] Some examples involving binuclear methyl complexes have been found to yield acetone but not the doubly carbonylated product 2,3-butanedione.[2] The formation of butanedione is relatively rare and has been seen in the carbonylation of $Ni(CH_3)_2(bpy)$, the photolysis of $(\eta^5\text{-Cp})Re(CH_3)(COCH_3)(CO)_2$ under 20 atm of CO, and the carbonylation of $Pd(CH_3)_2L_2$ (L = phosphine) in low yield.[3-5] In this communication, we report the synthesis and characterization of a dimethyl A-frame complex of rhodium and its carbonylation chemistry, which leads to acetone and 2,3-butanedione by different mechanisms with a balance between the carbonylation pathways that is extraordinary.

The complex $Rh_2(\mu\text{-CO})(CH_3)_2(dppm)_2$ (**1**; dppm = bis(diphenylphosphino)methane) is synthesized by the reaction of $Rh_2(CO)_2Cl_2(dppm)_2$[6] with methylmagnesium chloride in THF at −75 °C under nitrogen. The orange, air-sensitive product is recrystallized from THF or benzene and characterized spectroscopically. The infrared spectrum of **1** shows a single ν_{CO} at 1728 cm^{-1} assignable to a bridging carbonyl. In the ^1H NMR spectrum of **1** in C_6D_6, methylene resonances occur as doublets of multiplets at δ 3.25 and 3.65 ppm, indicating an inequivalency of protons on the same dppm, while the methyl resonance appears at δ 0.35 ppm as a broad singlet due to unresolved J_{Rh-H} and J_{P-H} coupling. The $^{31}P\{^1H\}$ NMR spectrum exhibits a second-order pattern (AA′XX′X″X‴) (see Figure 1a), which can be simulated with coupling constants consistent with an A-frame structure having a large trans J_{P-Rh-P} coupling of 350.0 Hz (Figure 1b).[7,8]

When **1** is labeled with ^{13}CO, the carbonyl resonance in the ^{13}C NMR spectrum is a triplet of quintets at δ 236.6 ppm, indicating coupling to equivalent Rh and P nuclei. The $^{31}P\{^1H\}$ NMR spectrum of this labeled compound (Figure 1c) possesses

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(7) ^1H NMR (δ, C_6D_6, Me_4Si): 0.35 br s (CH_3), 3.25 m (*H*CH), 3.65 m (HC*H*), 6.90 m (p,m-phenyl), 7.65 s (o-phenyl). ^{13}C NMR (δ, C_6D_6, Me_4Si): $Rh_2(\mu\text{-CO})(^{13}CH_3)_2(dppm)_2$, 3.8 (second-order pattern); $Rh_2(\mu\text{-}^{13}CO)(CH_3)_2(dppm)_2$, 236.6 t of quin ($^1J_{C-Rh}$ = 34.0 Hz, $^2J_{C-P}$ = 7.4 Hz). ^{31}P NMR (δ, C_6D_6, H_3PO_4): 32.5 (second-order pattern).

(8) Simulations were performed on a Bruker Aspect X32 using DSYMUX. ^{31}P simulation (AA′XX′X″X‴): $^2J_{P-Rh-P}$ = 350.0 Hz, $^2J_{P-C-P}$ = 95.0 Hz, $^3J_{P-P}$ = 14.5 Hz, $^1J_{Rh-P}$ = 156.5 Hz, $^2J_{Rh-P}$ = −1.2 Hz. Simulation for **1**-^{13}CO (AA′MXX′X″X‴): $^2J_{P-Rh-P}$ = 350.0 Hz, $^2J_{P-C-P}$ = 95.0 Hz, $^3J_{P-P}$ = 14.5 Hz, $^1J_{Rh-P}$ = 156.5 Hz, $^2J_{Rh-P}$ = −1.2 Hz, $^1J_{C-Rh}$ = 34.0 Hz, $^2J_{C-P}$ = 7.4 Hz.

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