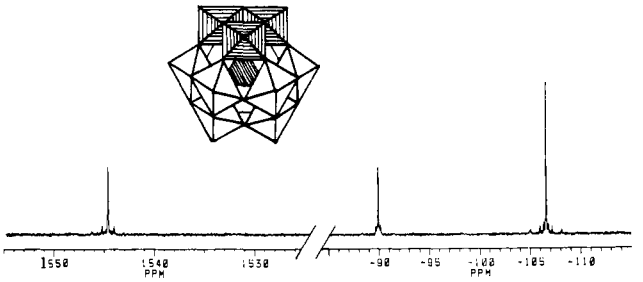

Figure 1. ^{183}W NMR spectrum, 12.505 MHz, of 0.15 M $H_4[SiW_{12}O_{40}H_6]$ in 0.5 M DCl. The W(IV) atoms occupy the crosshatched octahedra in the Keggin structure shown.

Table I. ^{183}W NMR Data for Oxidized and 6-Electron Reduced $[XW_{12}O_{40}]^{n-}$ [a]

anion	chemical shift/ppm[b]	$^2J_{W-W}$/Hz[c]	line width/Hz[d]
$SiW_{12}O_{40}^{4-}$	−102.5		0.3
$SiW_{12}O_{40}H_6^{4-}$	+1544.6 (3 W)	15.1	1.2
	−89.9 (3 W)	6.4	0.9
	−106.6 (6 W)	6.4, 15.0	0.9
$BW_{12}O_{40}^{5-}$	−128.5		1.1
$BW_{12}O_{40}H_6^{5-}$	+1452.8 (3 W)	14.4	2.3
	−107.4 (3 W)	4.2	1.2
	−131.6 (6 W)	4.2, 14.4	1.0
$(H_2)W_{12}O_{40}^{6-}$	−109.5		2.3
$(H_2)W_{12}O_{40}H_6^{6-}$	+1355.4 (3 W)[e]	*f*	1.6
	−82.0 (3 W)	*f*	1.6
	−115.0 (6 W)	*f*, 14.6	2.9
$W_3O_4(H_2O)_9^{4+}$	+1138.4		3.0[g]

[a] In 0.5 M DCl. [b] ±0.1 ppm. [c] ±0.5 Hz. [d] ±0.1 Hz. [e] Resonances for HD and D_2 isotopomers are also observed; see text. [f] Coupling is not resolved. [g] In saturated *p*-toluenesulfonic acid.

exchange of H by D occurs and the resonances of the three isotopomers with internal H_2^{2+}, HD^{2+}, and D_2^{2+} are resolved at 1355.4, 1354.8, and 1354.3 ppm, respectively.[16] The corresponding effects of deuteration upon the two W(VI) resonances are not observed although these two lines are slightly broadened (Table I). These data, coupled with a much smaller isotope effect for the oxidized metatungstate anion,[17] suggest that the internal protons in the reduced anion are both covalently attached to $O(W^{IV})_3$, i.e., that this oxygen atom has become a water molecule.[18] Tourné, Tourné, and Weakley[19] have demonstrated isotope effects of a similar magnitude and direction for the resonances of a tungsten atom bound to an "internal" water molecule of $P_2W_{21}O_{71}(OH_2)_3^{6-}$.

Acknowledgment. We thank Dr. T. J. R. Weakley for preprints of ref 19 and Dr. R. Acerete for information regarding his current work. This research has been supported by NSF Grants CHE-8306736 and CHE-8406088 and by an instrument grant from the Keck foundation.

(16) Assignment of the three lines was confirmed by allowing the reduced solution to undergo (very slow) further exchange over a period of 2 months.

(17) Acerete et al. (Acerete, R.; Hammer, C. F.; Baker, L. C. W. *J. Am. Chem. Soc.* **1982**, *104*, 5384) tentatively proposed rapid, pH-dependent H–D exchange for $(H_2)W_{12}O_{40}^{6-}$ and concluded that $\Delta\delta_W$ for $(H_2)W_{12}O_{40}^{6-}$ and $(D_2)W_{12}O_{40}^{6-}$ was −7 ppm. It now appears that the original data reflect external protonation effects only (Acerete, private communication). We have synthesized $(D_2)W_{12}O_{40}^{6-}$. Spectra of mixtures of $(D_2)W_{12}O_{40}^{6-}$ and $(H_2)W_{12}O_{40}^{6-}$ show two lines separated by 0.1 ppm. The deuterio anion has the more highly shielded resonance.

(18) It is reasonable to expect that the oxygen bonded to the W(IV) triad would be the most basic of the interior oxygens. Chauveau et al. (Chauveau, F.; Doppelt, P.; Lefebvre, J. *Bull. Soc. Chim. Fr.* **1983**, 197) propose just the opposite, i.e., preferential protonation of W(VI) oxygens, based on ^1H and ^{19}F NMR of reduced fluorotungstates, $[H_2W_{12}F_nO_{40-n}]^{(6-n)}$ (n = 1–3). However, the data of Chauveau et al. are equally consistent with our suggestion.

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Stereocontrolled Total Synthesis of (±)-Cyanocycline A

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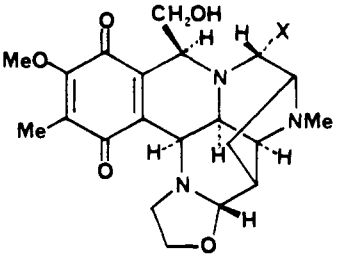
Cyanocycline A (**1**) was isolated from the fermentation broth of *Streptomyces flavogriseus* and has been shown to exhibit broad-spectrum antimicrobial and antitumor activities.[1] The structure of **1** was determined by an X-ray crystallographic analysis and was found to be identical with cyanonaphthyridinomycin,[2] which was derived from naphthyridinomycin[3] (**2**) by treatment with sodium cyanide. The challenging



1: X = CN

2: X = OH

synthetic problems of **1** involve controlling stereochemistry of the eight chiral centers of the highly crowded hexacyclic system, in addition to the construction of such labile functional groups as quinone and oxazolidine. The first total synthesis of this formidable molecule has recently been achieved by Evans and his co-workers.[4] In this paper we describe a stereocontrolled total synthesis of cyanocycline A (**1**), which is the result of our intensive efforts directed toward syntheses of this class of quinone antitumor antibiotics.[5]

One of the key reactions of our synthesis is an addition of zinc dienolate derived from the dihydropyrrole **3**[6,7] to 5-(benzyloxy)-2,4-dimethoxy-3-methylbenzaldehyde (**4**)[5a] (THF, 0 °C, 30 min), which gave a diastereomeric mixture of the thermodynamically favorable γ-addition products **5** in 77% yield. Hydrogenolysis of benzyl ether (H_2 (1000 psi), 10% Pd/C, EtOH, room temperature, 96%) followed by hydrogenation of olefin (H_2 (1500 psi), 5% Rh/C, EtOAc, 80 °C, 100 min, 63%) gave the pyrrolidine **6**. Stereochemistry of the pyrrolidine ring **6** was completely controlled as evidenced by the formation of the keto ester **7** as the single isomer in a three-step sequence ((1) $PhCH_2Br$, K_2CO_3, acetone, reflux; (2) Jones oxidation, acetone, 0 °C; (3) MeI,

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(6) Prepared from *N*-*t*-Boc-dehydroalanine-*tert*-butyl ester (i) in a three-step sequence in 68% overall yield: (1) i, *tert*-butyl acetoacetate (1.5 equiv), NaOEt (0.2 equiv), EtOH, 60 °C; (2) p-TsOH (0.3 equiv), quinoline (0.6 equiv), toluene, Dean–Stark trap, reflux; (3) $LiBEt_3H$ (2.2 equiv), THF, −20 °C.

(7) Satisfactory spectroscopic data were obtained for each intermediate.

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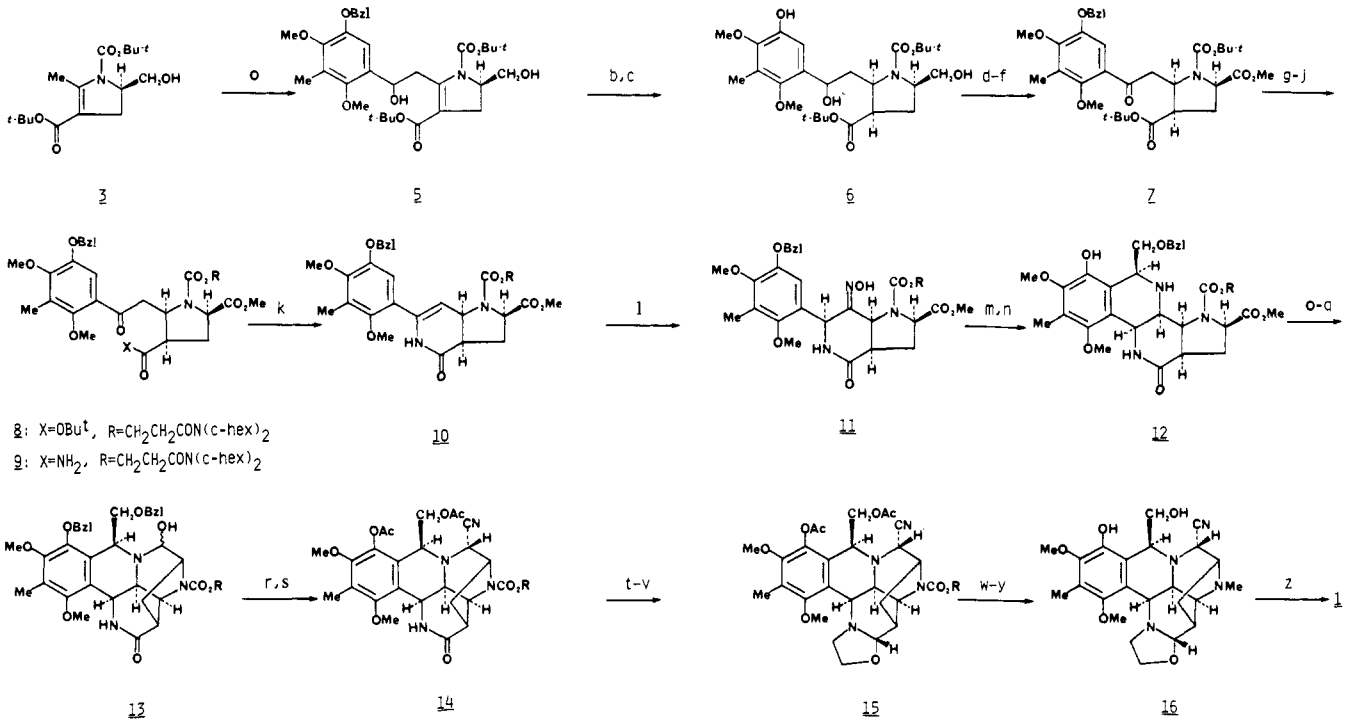
Scheme I[a]



[a] (a) LDA (2.5 equiv), THF, −78 °C, 15 min, then 1.5 M $ZnCl_2$/THF (2 equiv) followed by **4**, −78 to 0 °C, 30 min. (b) H_2 (1000 psi), 10% Pd/C, EtOH, room temperature, 5 h. (c) H_2 (1500 psi), 5% Rh/C, EtOAc, 80 °C, 100 min. (d) $PhCH_2Br$, K_2CO_3, acetone, reflux, 40 min. (e) Jones oxidation, acetone, 0 °C, 1 h. (f) MeI, K_2CO_3, acetone, reflux, 30 min. (g) 2% TFA–CH_2Cl_2, reflux, 3 h. (h) $ClCO_2CH_2CH_2CON(c\text{-hex})_2$, *i*-$Pr_2NEt$, CH_2Cl_2, 0 °C, 15 min. (i) TFA, room temperature, 20 min. (j) $ClCO_2Et$ (4 equiv), Et_3N (3 equiv), CH_2Cl_2, 0 °C, 5 min, then NH_3, CH_2Cl_2, 0 °C, 10 min. (k) CSA (0.6 equiv), quinoline (1.2 equiv), benzene, reflux, 40 min. (l) NOCl, CH_2Cl_2–CH_3CN (2:1), −35 °C, then MeOH, $NaBH_3CN$, −20 °C, 30 min. (m) H_2 (1500 psi), Ra–Ni (W-2), Et_3N (1 equiv), EtOH, 100 °C, 30 min. (n) $PhCH_2OCH_2CHO$ (15 equiv), AcOH (2 equiv), MeOH, 60 °C, 90 min. (o) $PhCH_2Br$, K_2CO_3, DMF, 50 °C, 30 min. (p) $LiBEt_3H$, TMEDA (4 equiv), THF, 0 °C. (q) Swern oxidation.[10] (r) Me_3SiCN, $ZnCl_2$, CH_2Cl_2, room temperature, 1 h. (s) BCl_3, CH_2Cl_2, 0 °C, then MeOH, evaporation, Ac_2O, Py, RT, 2 h. (t) Lawesson's reagent, benzene, 80 °C, 30 min. (u) Ra–Ni (W-2, washed with acetone), acetone, room temperature, 80 min. (v) ethylene oxide–MeOH (1:1), 60 °C, 4 h. (w) 3 N NaOH, MeOH, room temperature. (x) 1 M *t*-BuOK/*t*-BuOH (3 equiv), 18-crown-6 (1 equiv), THF, 0 °C, 30 min. (y) MeI (10 equiv), *i*-Pr_2NEt (30 equiv), CH_3CN, 60 °C, 60 h. (z) $Mn(OAc)_3$ (excess), 0.3% H_2SO_4–CH_3CN, room temperature, 2 h.

K_2CO_3, acetone, reflux) in 80% overall yield. Earlier model studies have suggested that we need to devise a novel amino protecting group which can survive acidic (TFA, room temperature), basic (3 N NaOH, MeOH, room temperature), and reductive ($LiAlH_4$, ether, 0 °C; H_2 (1500 psi), Ra-Ni (W-2), EtOH, 100 °C) conditions and yet can be deprotected under reasonably mild conditions. After numerous attempts, we have finally found one that meets such demanding requirements. Thus *N*-Boc group of **7** was selectively deprotected (2% TFA–CH_2Cl_2, reflux) and the resulting amine was treated with *N*,*N*-dicyclohexyl-3-chlorocarboxypropanamide[8] (*i*-Pr_2NEt, CH_2Cl_2, 0 °C) to give the urethane **8** in 77% yield. The *tert*-butyl ester **8** was converted to the amide **9** in a conventional manner ((1) TFA, room temperature; (2) $ClCO_2Et$, Et_3N, CH_2Cl_2, 0 °C, then NH_3 at 0 °C) in 94% yield. The critical cyclization of the keto amide **9** furnished the ene lactam **10** in 85% yield (CSA (0.6 equiv), quinoline (1.2 equiv), benzene, reflux, 40 min)[9] (Scheme I).

Undoubtedly, the most important step in our synthesis is the stereoselective conversion of the ene lactam **10** to the oxime **11**. This vital transformation was accomplished by oxidation with nitrosyl chloride (CH_2Cl_2–CH_3CN (2:1), −35 °C) followed by in situ reduction of the resultant α-chloro oxime ($NaBH_3CN$, MeOH, −20 °C) to give predominantly the desired oxime **11** in 64% yield. Catalytic hydrogenation of the oxime **11** occurred exclusively from the less hindered, convex face of the molecule to yield the aminophenol (H_2 (1500 psi), Ra–Ni (W-2), Et_3N (1 equiv), EtOH, 100 °C, 30 min, 72%), which gave the tetrahydroisoquinoline **12** as the sole product upon treatment with glycolaldehyde benzyl ether (AcOH (2 equiv), MeOH, 60 °C, 92%). Protection of phenol ($PhCH_2Br$, K_2CO_3, DMF, 50 °C, 92%), reduction of methyl ester ($LiBEt_3H$, TMEDA (4 equiv), THF, 0 °C, 76%), and subsequent Swern oxidation[10] of the resultant alcohol gave the aminal **13** (85%). The epimeric mixture of the aminal **13** afforded the single isomer of aminonitrile upon treatment with trimethylsilyl cyanide ($ZnCl_2$, CH_2Cl_2, room temperature, 89%). Since hydrogenolysis of the benzyl ethers in the later stage was unsuccessful, the acetate **14** was employed for protection of the hydroxy groups ((1) BCl_3, CH_2Cl_2, 0 °C, 82%; (2) Ac_2O, Py, room temperature, 86%). Facile conversion of the lactam **14** to the oxazolidine **15** was carried out in the following manner. Upon treatment with Lawesson's reagent[11] (benzene, 80 °C), **14** gave the thiolactam in 85% yield. Careful desulfurization of the thiolactam furnished directly the stable imine (Ra–Ni (W-2), acetone, room temperature, 87%), which was converted to the oxazolidine **15** by using Pelletier's procedure[12] (ethylene oxide–MeOH (1:1), 60 °C, 4 h, 99%). Hydrolysis of the acetate **15** (3 N NaOH, MeOH, room temperature, 100%), deprotection of the amino protecting group (*t*-BuOK/*t*-BuOH (3 equiv), 18-crown-6 (1 equiv), THF, 0 °C, 30 min, 100%), and methylation of the amine gave **16** (MeI, *i*-Pr_2NEt, CH_3CN, 60 °C, 77%). Finally, oxidation of the phenol **16** with manganese triacetate (0.3% H_2SO_4–CH_3CN, room temperature) afforded highly crystalline, synthetic cyanocycline A (**1**) in 55% yield.[13]

(8) Synthesized in 80% overall yield in a three-step sequence: (1) acryloyl chloride, dicyclohexylamine, CH_2Cl_2, 0 °C; (2) $Hg(OAc)_2$, THF–H_2O (3:1), reflux, 10 h; (3) $COCl_2$, THF, 0 °C.

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The synthetic cyanocycline A[14] was identical with an authentic sample in TLC behavior and spectroscopic properties.[15]

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Supplementary Material Available: Copies of NMR spectra of key intermediates and synthetic cyanocycline A (9 pages). Ordering information is given on any current masthead page.

(13) All the other oxidation conditions we tried furnished no more than 25% yield of **1**.
(14) The yellow crystals started darkening at 140 °C and became a black mass by 160 °C without showing clear melting point.
(15) We are indebted to Professor Steven Gould, Oregon State University, for a sample of authentic cyanocycline A.

Dual Emission from an Ortho-Metalated Ir(III) Complex

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Several complexes of Ir(III) containing both the bidentate N-coordinating ligand 2,2′-bipyridine (bpy) and the N,C-ortho-metalating ligand 2-phenylpyridine (ppy) have recently been prepared; these include the two species $Ir(ppy)_2(bpy)^+$ (A) and $Ir(ppy)(bpy)_2^{2+}$ (B). The former was prepared from the dichloro-bridged dimer, $[Ir(ppy)_2Cl]_2$, by modification of the procedure of Nonoyama[1,2] while the latter was obtained by reaction[3] of *cis*-$[Ir(bpy)_2(OSO_2CF_3)_2][CF_3SO_3]$ with ppy in refluxing 2-ethoxyethanol. Both complexes were purified by column chromatography on Sephadex LH-20 using ethanol for elution. The purity of the complexes was monitored with thin-layer chromatography using silica gel plates and 1:1:1 acetone/methanol/water mixtures for elution. Samples of the complexes used in these studies showed only one component in thin-layer chromatography. While only one isomer of B is possible, there are three possible isomers of A. Data from ^1H and ^{13}C NMR experiments[4] indicate that A has C_2 symmetry. The NMR spectrum indicates, as does thin-layer chromatography, that only a single isomer of A is present with no detectable impurities due to a mixture of isomers. While X-ray structural data for A are lacking, structural data for related complexes[5-8] suggest that A is the isomer with cisoid metal–carbon bonds and bpy metal–nitrogen bonds transoid to the metal–carbon bonds. These species were prepared in order to probe further the effects of metal–carbon bonding on energy-transfer processes and electron-transfer reactions of metal complexes.[9,10] Emission spectroscopic studies reported here reveal unusual and distinct intramolecular energy-transfer behavior in these complexes. Whereas dual emission from the former is observed in glasses at 77 K, a single emission is observed in the latter.

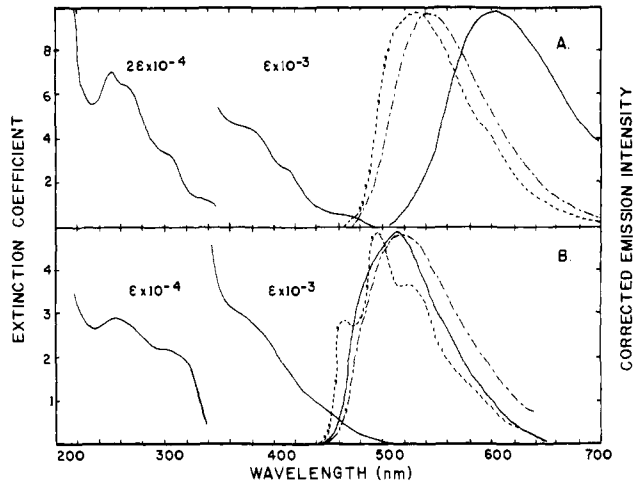

Figure 1. Absorption and emission spectra of $Ir(ppy)_2(bpy)^+$ (A) and of $Ir(bpy)_2(ppy)^{2+}$ (B). A: (—) absorption (left) and emission (right) in methanol at room temperature; (- - -) emission in ethanol/methanol (4:1 by volume) at 77 K; (-·-·-) emission in poly(methyl methacrylate) at room temperature. B: (—) absorption (left) and emission (right) in methanol at room temperature; (- - -) emission in ethanol/methanol (4:1 by volume) at 77 K; (-·-·-) emission in poly(methyl methacrylate) at room temperature.

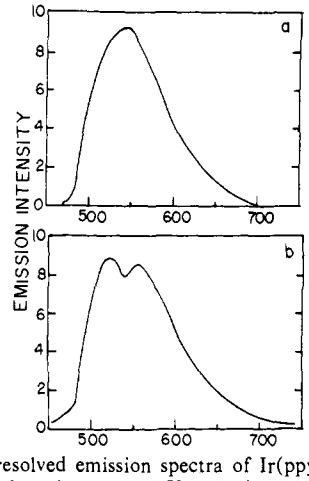

Figure 2. Time-resolved emission spectra of $Ir(ppy)_2(bpy)^+$ in ethanol/methanol (4:1 by volume) at 77 K excited at 336 nm with a pulsed nitrogen laser: (a) 100 ns after excitation; (b) 15 μs after excitation.

The absorption spectra of A and B at room temperature and their time-integrated emission spectra in fluid solutions at room temperature and in 77 K glasses are presented in Figure 1. The broad, structureless emission spectrum of A in 77 K glasses contrasts with the structured emission of B, as does the large red shift of the emission of A in fluid room temperature solutions relative to the small red shift of B. That this is largely a viscosity effect rather than a temperature effect is evidenced by observations of comparable red shifts in the emissions of A and B in 77 K and room temperature poly(methyl methacrylate) solutions.

The emission lifetimes of A and B are comparable in 77 K ethanol–methanol glasses (5.0 and 6.8 μs, respectively) and in fluid room temperature methanol solutions (0.35 and 1.1 μs, respectively). Luminescence decay curves of both complexes excited with the 337-nm fundamental of the N_2 laser at 77 K fit sufficiently well to a single exponential analysis to indicate that, if two components are emissive, their lifetimes are similar. Attempts to fit the luminescence decay data for A to a double-exponential

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