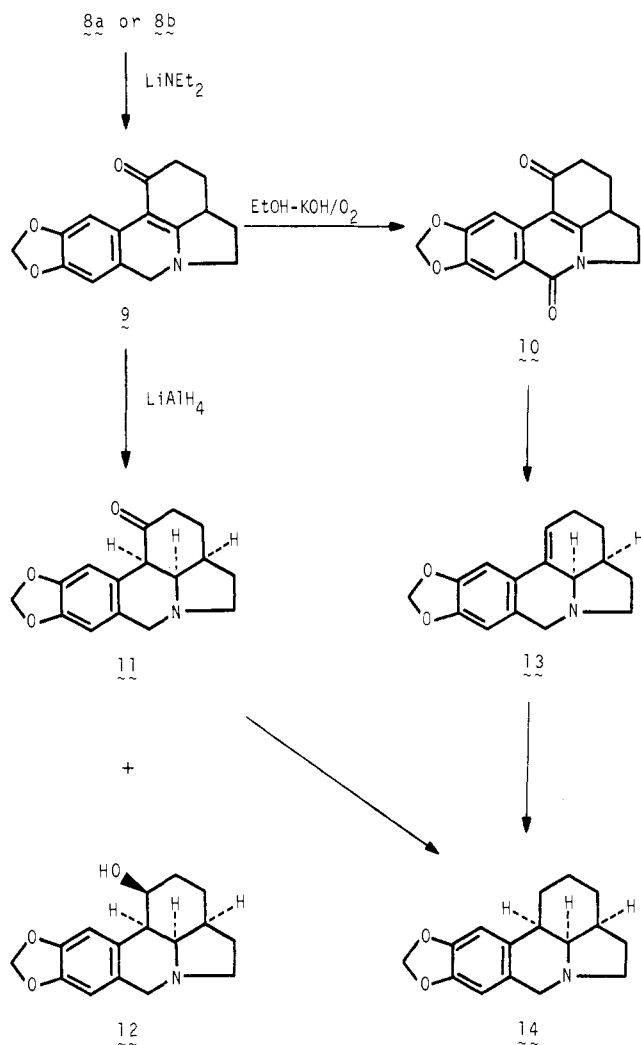


enaminone **8a** in 51% yield: mp 157–158 °C; IR (CHCl₃) 1605 (C=O),⁵ 1580 cm⁻¹ (C=C);⁵ NMR (CDCl₃) δ 5.10⁵ (s, 1 H). Similar treatment of **6** with **7b** yielded the corresponding iodoenaminone **8b** in 50% yield: mp 173–174 °C; IR (CHCl₃) 1605, 1580 cm⁻¹; NMR (CDCl₃) δ 5.09 (s, 1 H).

The ring closure of the bromoenaminone **8a** was successfully carried out in a similar manner to that described above. The reaction proceeded to completion in 30 min at room temperature, giving the pyrrolophenanthridone **9** in 49% yield: IR (CHCl₃) 1610, 1560 cm⁻¹; NMR (CDCl₃) δ 4.53 (s, 2 H, CH₂Ph), 5.87 (s, 2 H, OCH₂O), 6.34 (s, 1 H, 8-H), 8.52 (s, 1 H, 12-H). In the same manner the cyclization of the iodoenaminone **8b** afforded **9** in 35% yield. This product began to



melt at 145 °C and completely liquefied at 252 °C coinciding with the melting point reported for the keto lactam **10**,^{4,6,7} which suggested that **9** would be susceptible to air oxidation to **10**. Accordingly, **9** was treated with oxygen in ethanol containing aqueous KOH to give the keto lactam **10**, mp 252–253 °C, directly identical in all respect with an authentic sample.⁴ Compound **10** can be readily converted into (\pm)- γ -lycorane (**14**) via (\pm)- α -anhydrodihydrocaranone (**13**) according to a procedure previously reported.⁴

On the other hand, reduction of **9** with LiAlH₄ in THF at room temperature stereoselectively provided (\pm)- α -dihydrocaranone (**11**) in 33% yield (mp 147–149 °C (lit.⁸ mp 147.5–149.5 °C); IR (CHCl₃) 1705 cm⁻¹; NMR (CDCl₃) δ 3.29 and 4.00 (AB q, *J* = 14 Hz, CH₂Ph), 3.47 (d, *J* = 4 Hz, 1 H, 12b-H), 5.89 (s, 2 H, OCH₂O), 6.49 (s, 1 H, 8-H), 6.59 (s, 1 H, 12-H)) and (\pm)-1-epi- γ -dihydrocaranone (**12**) in 10% yield (mp 134–135 °C (lit.⁸ mp 135.5–136.5 °C); IR (CHCl₃)

3250 cm⁻¹; NMR (CDCl₃) δ 3.28 and 4.04 (AB q, *J* = 14 Hz, CH₂Ph), 5.09 (s, 2 H, OCH₂O), 6.48 (s, 1 H, 8-H), 6.64 (s, 1 H, 12-H)). The IR and NMR spectra of these products were superimposable on those of authentic materials.⁹ Conversion of α -dihydrocaranone (**11**) into γ -lycorane (**14**) has been achieved.^{8,10}

References and Notes

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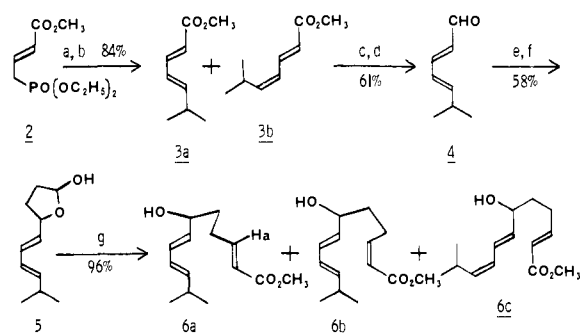
Total Synthesis of (\pm)-Dendrobine¹

Sir:

Dendrobine (**1**), the major component of the Chinese drug "Chin-Shih-Hu", has been the subject of recent synthetic investigations, in part as a consequence of its structural and pharmacological similarities to picrotoxinin.² Herein we describe a total synthesis³ of this alkaloid by a highly stereoselective route which utilizes an intramolecular Diels-Alder reaction⁴ as the key skeleton-forming transformation.⁵

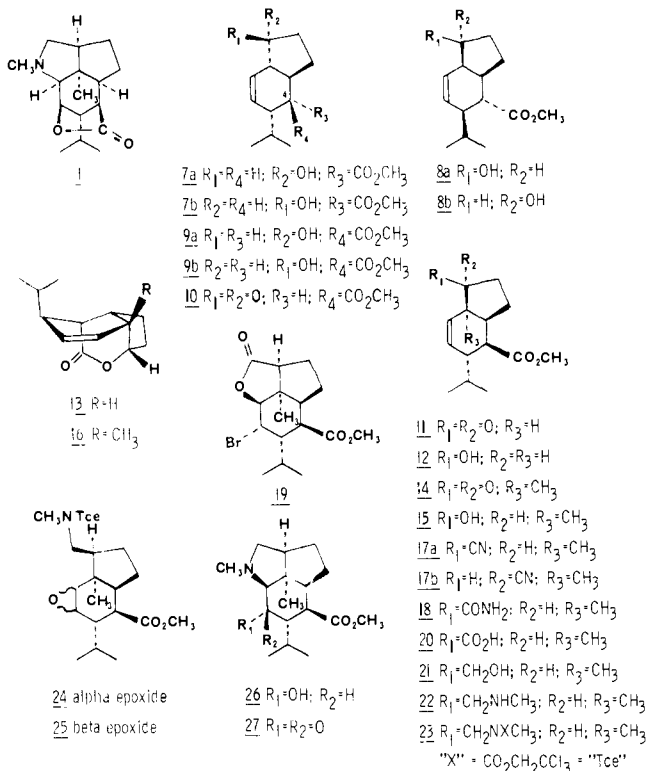
The synthesis of the Diels-Alder substrate **6a** was achieved as described in Scheme I. The mixture of dienes **3** obtained from condensation of the stabilized anion of **2** with isobutyraldehyde⁷ contained 93% **3a**.^{6a,8} The trans,trans stereochemistries of **3a** and **4**^{6a,b} were assigned on the basis of their characteristic NMR and UV spectra, which were similar to those of methyl sorbate and sorbaldehyde, respectively.⁹ Careful chromatography of the triene mixture (96% crude) obtained

Scheme I



^a TMS₂NLi, THF, -78 °C. ^b Isobutyraldehyde, -40 °C. ^c Dibal, Et₂O. ^d CrO₃-py. ^e BrMgCH₂CH₂CHOCH₂CH₂O-, THF. ^f THF, aqueous HCl. ^g Carbomethoxymethylenetriphenylphosphorane, CH₂Cl₂.

from hemiacetal **5**^{6a,c} by the Wittig reaction¹⁰ provided pure **6a**^{6a,b} in 82% yield along with small amounts of **6b**^{6a,b} (5%) and **6c**^{6a,c,11} (0.6%). The ¹H NMR spectrum of **6a** clearly showed that the dienophilic double bond was trans (H_a , 6.98 (dt, $J = 16, 7$ Hz)).¹²



Cyclization of **6a** by refluxing a 0.2 M toluene solution of the corresponding trimethylsilyl ether (formed in situ with 1.2 equiv of BSA,¹³ 23 °C, 7 h) for 85 h afforded four perhydroindanols in 83% yield after acid hydrolysis (MeOH, 1 N HCl, 23 °C, 15 min) and silica gel chromatography: **7a**,^{6a,b} mp 53–54 °C (39%); **7b**,^{6a,b} mp 76–77 °C (33.5%); **8a**^{6a,c} (1%); and **8b**,^{6a,b} mp 72–76 °C (9.5%). Treatment of either **7a** or **7b** with 3–5 equiv of NaOMe in MeOH at 110 °C for 20–24 h resulted in partial epimerization of the C₄ carbomethoxyl groups. Thus, **7a** yielded 67% **9a**^{6a,b} (80% based upon unrecovered **7a**) and **7b** gave 68% **9b**^{6a,b} (77% based upon unrecovered **7b**). Oxidation of either **9a** or **9b** with Swern's TFAA–Me₂SO reagent¹⁴ afforded in high yield a crude, unstable ketone **10** which upon silica gel chromatography isomerized to **11**,^{6a,b} mp 69–71 °C. The yield of **11** was 91% from **9a** and 84% from **9b**. Reduction of **11** with NaBH₄ in EtOH afforded a single alcohol **12**,^{6a,b} mp 76–77 °C (73%), which upon treatment with TFA in CH₂Cl₂ (23 °C, 2 days) resulted in formation of lactone **13**^{6a,c} (73%). Hence, **11** and **12** possess *cis*-perhydroindan skeletons.

Angular methylation of **11** (1.0 equiv of KO-*t*-Bu, excess CH₃I, DME, *t*-BuOH) afforded a single alkylation product, **14**,^{6a,b} mp 91–93 °C (95%), which was shown to possess a *cis*-ring fusion by NaBH₄ reduction (giving a single alcohol, **15**,^{6a,b} mp 83–87 °C) and TFA catalyzed lactonization to give 73% **16**,^{6a,b} mp 55–56 °C. Reductive cyanation of **14** (TosMIC, KO-*t*-Bu, DME, *t*-BuOH)¹⁵ afforded a major nitrile **17a**,^{6a,b} mp 47–51 °C (41.5%; NMR δ 1.26 (3 H, s)) along with a minor nitrile **17b**,^{6a,b} mp 90–91 °C (10.6%; NMR δ (1.35 (3 H, s)).¹⁶ Hydrolysis of **17a** (H₂O₂, NaOH, EtOH, 98%)¹⁷ afforded an amide **18**,^{6a,b} mp 185–186 °C, which was oxidized with NBS in wet THF containing HOAc¹⁸ to give bromolactone **19**,^{6a,b} mp 107–108 °C, in 86% overall yield. Reduction of **19** with Zn in refluxing HOAc¹⁹ followed by

sequential treatment of acid **20**^{6a,b} (mp 112–113 °C) with oxalyl chloride and lithium tri-*tert*-butoxyaluminum hydride²⁰ in THF at 0 °C gave 90% **21**,^{6a,c} mp 72–73 °C. Mesylation²¹ of **21** followed by displacement with CH₃NH₂ (Me₂SO, 85 °C, 18 h) provided 83% amine **22**,^{6a,c}

Treatment of **22** with trichloroethyl chloroformate and pyridine in CH₂Cl₂²² afforded 98% urethane **23**,^{6a,b} mp 90–91 °C, which was epoxidized (excess MCPBA, toluene, 120 °C, 2 h) in the presence of 4,4'-thiobis(6-*tert*-butyl-3-methylphenol)²³ giving 40% **24**,^{6a,b} mp 107.5–109 °C (NMR δ 1.20 (3 H, s)) and 47% **25** (NMR δ 1.15 (3 H, s)).²⁴ Deprotection (Zn, HOAc–DME)²² of **24** occurred with concomitant epoxide ring opening to afford 97% **26**^{6a,c} (NMR δ 3.67 (3 H, s), 2.11 (3 H, s), 1.33 (3 H, s), 1.01 and 0.97 (6 H, two d, $J = 6$ Hz)). Oxidation of **26** with excess Jones reagent at 0 °C gave 91% ketone **27** whose spectroscopic properties were identical with those reported by Kende.^{3c} Reduction of **27** (NaBH₄, isopropyl alcohol, 23 °C, 24 h) followed by silica gel chromatography gave 62% crystalline (\pm)-dendrobine,²⁵ mp 130–132 °C (lit. mp 131–132,^{3a} 128–130 °C^{3b}), whose relevant physical properties (¹H NMR (CDCl₃), IR (CH₂Cl₂), 70-eV mass spectra, TLC) were identical with those of a sample of the natural product.²⁶

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- chloroformate, pyridine, CH₂Cl₂.
 (25) Anal. Calcd for C₁₈H₂₅NO₃: C, 72.96; H, 9.57; N, 5.32. Found: C, 73.02; H, 9.65; N, 5.31.
 (26) We thank Professor K. Yamada for providing a generous sample of natural dendrobine used for comparative purposes.
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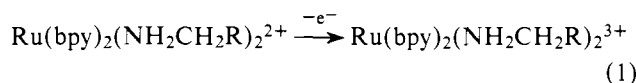
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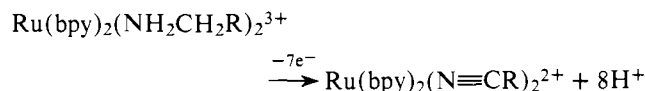
**Oxobis(2,2'-bipyridine)pyridineruthenium(IV) Ion,
 [(bpy)₂(py)Ru=O]²⁺**

Sir:

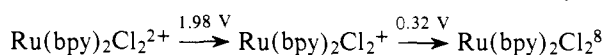
The earlier work of Dwyer and coworkers¹ and our more recent results have shown that for polypyridine complexes of ruthenium there is an extensive and reversible Ru(III)/Ru(II) redox chemistry.² This is especially true for *cis*-bis(2,2'-bipyridine) complexes where systematic changes in the remaining two inner coordination sphere ligands lead to predictable changes in redox potentials and charge-transfer spectra.² Polypyridine Ru(III)-Ru(II) couples have been of great value in studying electron-transfer processes in outer-sphere reactions,³ in mixed-valence complexes,⁴ and in reactions involving metal complex excited states.^{4,5} In some cases, Ru(III) complexes are unstable toward subsequent oxidation of a bound ligand (e.g., eq 1).⁶



In others Ru(IV) is an accessible oxidation state,

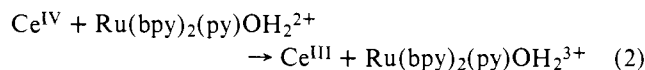


although with two bipyridine ligands only at high redox potentials as shown by the potentials below (vs. SCE) for the *cis*-dichloro Ru(IV)-Ru(III) and Ru(III)-Ru(II) couples.⁷



Complexes of Ru in high oxidation states are known. The preparations usually involve the addition of ligands to solutions containing RuO₄ and products form which contain both the added ligand and oxo groups. Examples include RuO₄py₂, [Ru(O)₂(NH₃)₄]Cl₂, and Cs₃[Ru(O)(CN)₄(CNO)₂].⁹ It is possible to show a direct connection between the lower and higher oxidation state chemistries of ruthenium using complexes which contain bound water or other ligands which have dissociable protons.

As shown by a spectrophotometric titration in 1.0 M HClO₄, the Ru(II) complex *cis*-Ru(bpy)₂(py)OH₂²⁺ (py is pyridine)¹⁰ is oxidized by Ce(IV) to Ru(III) (eq 2).

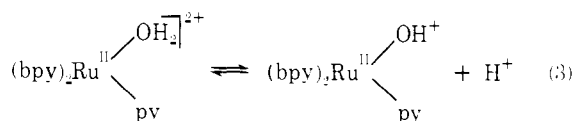


Upon oxidation, spectral changes occur which are typical for oxidation of Ru(II) to Ru(III):^{3b} (1) the π*(bpy) ← Ru(II) absorption band at λ_{max} 470 (ε 8400) disappears; (2) The pattern of π*(bpy) ← π(bpy) absorption bands in the ultraviolet changes predictably (λ_{max} 290 nm (ε 57 200) → λ_{max} 303 nm (ε 26 600) and 312 (26 200)). Surprisingly, however, we find that the Ru(III) complex undergoes a second one-electron oxidation by Ce(IV) to give a new species which has

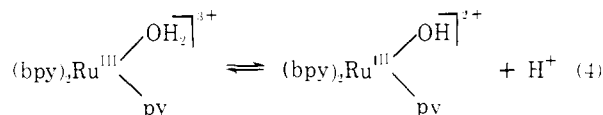
significant absorption bands only in the ultraviolet (λ_{max} 300 nm (ε 23 100), 248 (28 500)).¹¹

The twice-oxidized product precipitates from concentrated solutions as the perchlorate salt. Using the method of Feltham and Hayter,¹² conductivity studies in aqueous solution show that the cation has a +2 charge. In addition to the usual bpy and ClO₄⁻ bands in the infrared, a sharp intense band appears at 792 cm⁻¹ (Nujol mull) which is within the range expected (785–850 cm⁻¹) for a Ru=O stretching vibration.^{9a,13} The assignment of the band as ν(Ru=O) is supported by the shift of the band to 752 cm⁻¹ in the ¹⁸O-labeled complex (752 cm⁻¹ calculated). Magnetic susceptibility measurements on the salt at room temperature using the Faraday technique¹⁴ gave μ_{eff} = 2.95 μ_B which is slightly higher than the spin-only value for two unpaired spins (2.83 μ_B) and is consistent with the presence of a d⁴, paramagnetic Ru(IV) ion. Elemental analyses are consistent with the product being the perchlorate salt of the Ru(IV) complex (bpy)₂(py)Ru=O²⁺. Anal. Calcd for [Ru(bpy)₂(py)O](ClO₄)₂: C, 42.44; N, 9.90; H, 2.99. Found: C, 42.17; N, 9.85; H, 2.74.

We have investigated the acid-base and redox properties of the Ru(II)-Ru(III)-Ru(IV) system using spectral and electrochemical techniques (cyclic voltammetry, coulometry, and potentiometric titrations). A spectrophotometric titration shows that Ru(bpy)₂(py)OH₂²⁺ is a weak acid having pK_a (25 °C) ~10.8 in 0.333 M NaSO₄ (eq 3). In 1.0 M HClO₄, ox-



idation of Ru(bpy)₂(py)OH₂²⁺ at +0.90 V vs. the SCE (saturated calomel electrode) occurs with n = 1 (n is the electrochemical stoichiometry determined by coulometry) to give Ru(III) primarily as the aquo ion Ru(bpy)₂(py)OH₂³⁺. Rereduction of the Ru(III) complex to Ru(II) also occurs with n = 1. The Ru(III) complex is a strong acid, pK_a (25 °C) = 0.85 ± 0.03 in 1 M HClO₄/LiClO₄ (eq 4). Apparently, the



remarkably enhanced acidity following oxidation of Ru(II) to Ru(III) comes from stabilization of the electron-deficient Ru(III) site by p(OH⁻) → dπ(Ru(III)) electron donation. A new, intense absorption band appears for the hydroxo complex (λ_{max} 372 nm (ε 5560)) whose origin probably lies in a ligand to metal charge-transfer transition (dπ(Ru(III)) ← p(OH⁻)).¹⁵

Across the pH interval 0–7 in HClO₄/LiClO₄ solutions containing Ru(bpy)₂(py)OH₂²⁺, cyclic voltammograms (see Figure 1) show the expected Ru(III)/Ru(II) wave which is reversible and a Ru(IV)/Ru(III) wave which appears only at low scan rates. The difficulty with the Ru(IV)/Ru(III) wave is not understood. The peak to peak separation appears to be independent of sweep rate, but, at high sweep rates, both oxidation and reduction peaks disappear. The same effect is observed at Au wire and glassy carbon electrodes. In any case, coulometric oxidation of Ru(bpy)₂(py)H₂O²⁺ past the second wave occurs with n = 2 to give Ru(bpy)₂(py)O²⁺ which is rereduced to the Ru(II) complex with n = 2. Reduction potentials (uncorrected for activity coefficients) vs. the SCE were obtained for the two couples by a potentiometric titration using Ce(IV) in 1.0 M HClO₄. The values shown in eq 5 and 6 have been corrected for the partial deprotonation of Ru(bpy)₂(py)OH₂³⁺. Above pH 2, where Ru(bpy)₂(py)OH₂²⁺ is the dominant form of Ru(III), the Ru(IV)/Ru(III) and