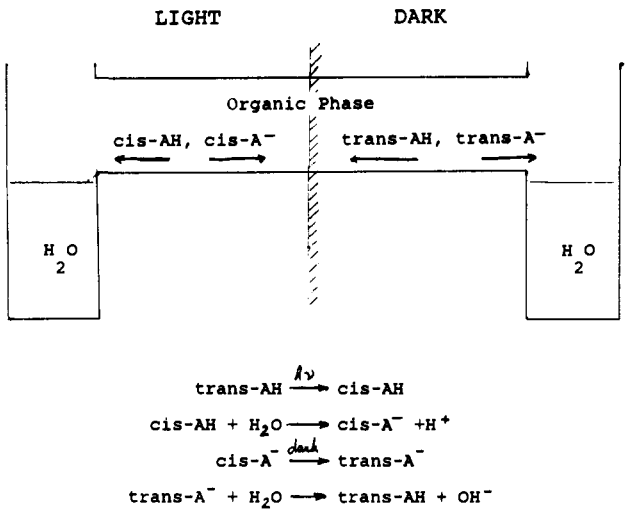

Figure 1. Schematic representation of light-powered proton transport across a liquid membrane.

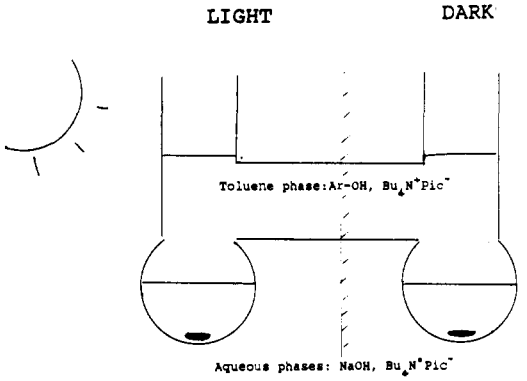

Figure 2. Liquid membrane.

to the aqueous phase. The complete scheme of reactions taking place in the liquid membrane is shown in eq 1–4.

$$trans\text{-}AH_{org} \xrightarrow{h\nu} cis\text{-}AH_{org} \quad (1)$$

$$cis\text{-}AH_{org} + NaOH_{aq} + Bu_4NPic_{org} \rightarrow cis\text{-}A^-Bu_4N^+_{org} + NaPic_{aq} + H_2O \quad (2)$$

$$cis\text{-}A^-Bu_4N^+_{org} \xrightarrow{dark} trans\text{-}A^-Bu_4N^+_{org} \quad (3)$$

$$trans\text{-}A^-Bu_4N^+_{org} + NaPic_{aq} + H_2O \rightarrow trans\text{-}AH_{org} + NaOH_{aq} + Bu_4NPic_{org} \quad (4)$$

After the *trans*-azophenol in the illuminated part of the organic phase is converted to the *cis*-azophenol (eq 1), it reacts with the aqueous NaOH forming a Bu_4N^+*cis*-A^- ion pair in the organic phase and forcing a Pic^- from the organic phase into the illuminated aqueous compartment (eq 2). The Bu_4N^+*cis*-A^- then reverts to Bu_4N^+-*trans*-A^- (eq 3) which then abstracts a proton from the H_2O in the dark aqueous compartment, generating an OH^- and allowing a Pic^- ion to enter the organic phase as $Bu_4N^+Pic^-$ (eq 4). The net result of each cycle is the appearance of one Pic^- and the disappearance of one OH^- from the illuminated aqueous compartment and the disappearance of one Pic^- and the appearance of one OH^- in the dark aqueous phase.

The liquid membrane consisted of two 100-mL, round-bottomed flasks joined by a bridge for the supernatant toluene solution (see Figure 2). Into the two round-bottomed flasks was poured 50 mL each of an aqueous solution containing 10^{-2} M NaOH, 1.18×10^{-4} M Bu_4N Pic, and 1.5 M Na_2SO_4. A toluene solution containing 6.17×10^{-4} M 2-hydroxy-3,5,6-trichloro-4′-methylazobenzene was then poured carefully on top to cover the two aqueous phases. The whole apparatus was immersed in a 25.0 °C constant temperature bath, the two flasks were subjected to vigorous stirring by means of two magnetic stirrers, and the left side of the liquid membrane was illuminated with a 275-W incandescent GE sunlamp. At the beginning of the experiment the contents of the two aqueous compartments were identical. At intervals aliquots of the two aqueous phases were assayed for picrate content. Figure 3 shows the increase in the picrate concentration of the illuminated aqueous compartment of the liquid membrane and the concomitant decrease in the picrate concentration on the dark side.[7] As can be seen from eq 1–4 the proton flux is exactly equal to changes in the picrate concentrations and is about 2×10^{-6} equiv per hour.

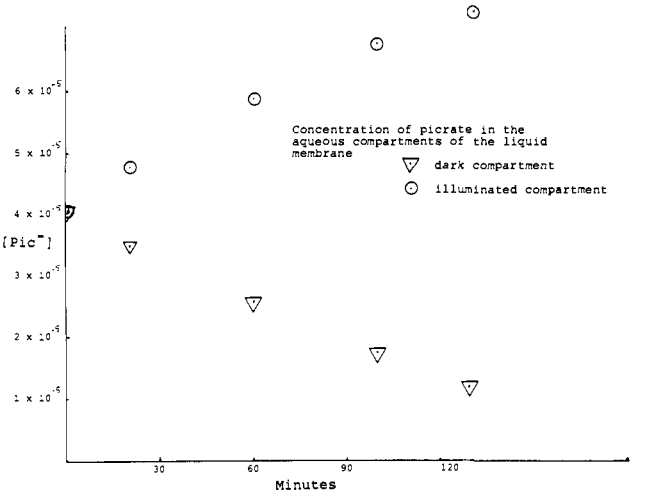

Figure 3. Change in the picrate concentration (M) in the illuminated and dark compartments of the liquid membrane vs. time (min).

Registry No. *trans*-AH, 109976-80-9; H_2O, 7732-18-5.

(7) The following controls should be noted: 1. When the illumination was placed on the other side of the liquid membrane the flow of picrate was reversed. 2. In the absence of illumination the two aqueous phases containing equal picrate concentrations maintained these concentrations without any change. No effort was made to exclude oxygen in these experiments.

The Biosynthetic Incorporation of [*methyl*-^{14}C,6-^{2}H,^{3}H]Trigonelline into Dioscorine in *Dioscorea hispida*

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Natural Products Laboratory,[1] Department of Chemistry University of Minnesota, Minneapolis, Minnesota 55455

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Dioscorine (**4**) is the main alkaloid found in the tropical yam *Dioscorea hispida* Dennstedt. We have previously established that this novel isoquinuclidine alkaloid is derived from nicotinic acid[2] (**1**) and acetic acid.[3] A biogenetic scheme for dioscorine was considered[2b] which involved a condensation between 3,6-dihydronicotinic acid (**2**) and a branched eight carbon unit **3** derived from four acetate units, one of the terminal carboxyl groups being ultimately lost in the formation of dioscorine. In order to probe this proposed biogenetic scheme, feeding experiments have been carried out with [6-^{14}C,2-^{3}H]nicotinic acid and [6-^{14}C,6-^{3}H]nicotinic acid.[4] Both these precursors were incor-

(1) Contribution no. 205 from this laboratory. Presented at the 4th International Conference on Chemistry and Biotechnology of Biologically Active Natural Products, Budapest, Hungary, August 10–14, 1987.

(2) (a) Leete, E. *J. Am. Chem. Soc.* **1977**, *99*, 648. (b) Leete, E. *Phytochemistry*, **1977**, *16*, 1705.

(3) Leete, E.; Pinder, A. R. *Phytochemistry* **1972**, *11*, 3219.

(4) These ^{3}H labeled nicotinic acids were prepared as previously described by Dawson et al. (Dawson, R. F.; Christman, D. R.; D'Adamo, A.; Solt, M. L.; Wolf, A. P. *J. Am. Chem. Soc.* **1960**, *82*, 2628.) and were mixed with commercially available (Amersham) [6-^{14}C]nicotinic acid prior to feeding.

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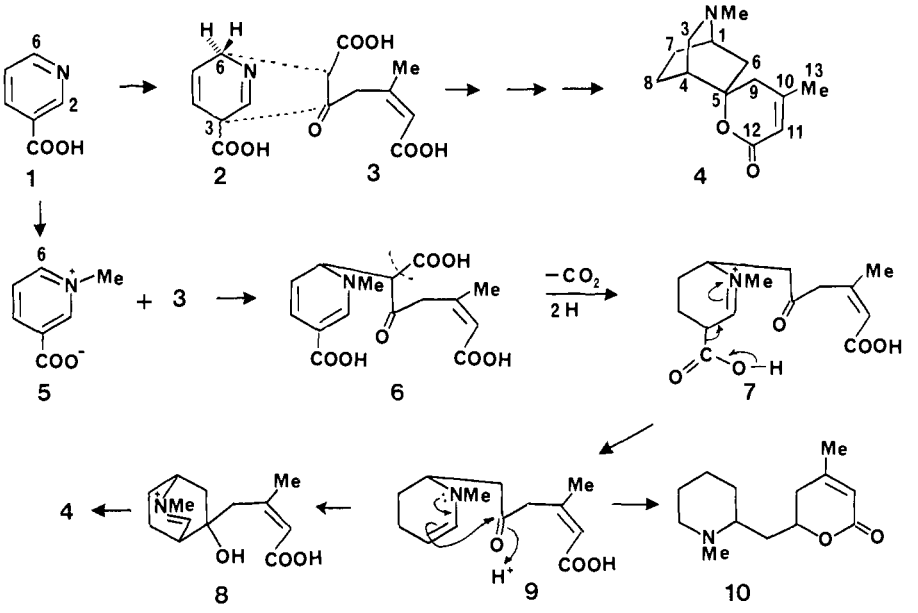
Table I. Incorporation of Precursors into Dioscorine

precursor	initial feeding data[a]	yield of dioscorine (mg)	% retntn of ^3H rel to ^{14}C	% incrprtn into dioscorine	
				Spec[b]	abs.[c]
[6-^{14}C,2-^{3}H]nicotinic acid 51.3 $^3H/^{14}C$ = 16.5	Sept 16, 1985	260	102	0.022	0.056
[6-^{14}C,6-^{3}H] nicotinic acid 53.4 mg $^3H/^{14}C$ = 9.53	Aug 14, 1985	641	104	0.53	3.51
[*methyl*-^{14}C,6-^{2}H,^{3}H] trigonelline 78.5 mg $^3H/^{14}C$ = 1.58	Oct 24, 1986	490	99	0.15	0.53

[a] All feedings were done by the cotton wick method, the initial administration of precursor, dissolved in water, being spread over 4 days, and then continued for a total of 5 weeks. [b] Specific inc. = dpm/mM (^{14}C) in dioscorine/dmp/mM (^{14}C) in precursor. [c] Absolute inc. = total activity (^{14}C) in dioscorine/total activity (^{14}C) in precursor.

Scheme I. New Hypothesis for the Biosynthesis of Dioscorine and Dumetorine



porated into dioscorine with complete retention of ^3H relative to ^{14}C (Table I).[5]

An alternative biosynthetic scheme, illustrated in Scheme I was considered in which nicotinic acid was activated by conversion to its betaine, trigonelline (**5**). Nucleophilic attack of the acetate-derived fragment at C-6 of trigonelline affords **6**. Reduction of the dihydropyridine ring with a shift of a double bond and decarboxylation of the β-keto acid yields **7**. Compound **9** arises by decarboxylation of the β-iminium carboxylic acid. The isoquinuclidine ring system is then formed by reaction of the enamine in **9** with the ketone, generating the hydroxy acid **8**. Reduction of the iminium ion and lactone formation then affords dioscorine. This new scheme differs from the previous one in that the bond which ultimately becomes 1–6 in dioscorine is formed before the 4–5 bond. This scheme also accommodates the alkaloid dumetorine (**10**) which has been found in a related species *Dioscorea dumetorum*.[6]

This new hypothesis has now been tested by feeding [*methyl*-^{14}C,6-^{2}H,^{3}H]trigonelline[7] to *D. hispida* plants. Deuterium was introduced at C-6 in the hopes that its incorporation into dioscorine could be monitored by ^2H NMR. A good incorporation (Table I) of the radioactive isotopes into dioscorine was obtained with almost complete retention of ^3H relative to ^{14}C. Before examination of the ^2H NMR of this labeled dioscorine, it was necessary to unequivocally assign the ^1H NMR spectrum of the alkaloid. This was done by examination of its 2D-HETCOR and 2D-COSY NMR. The HETCOR spectrum revealed that the hydrogen at C-1 (52.23 ppm in the ^{13}C NMR) has a chemical shift of 2.36 ppm (a pentet in an expanded spectrum). This 2D spectrum also indicated that the signals for C-6 and C-9 had been previously[2] misassigned, the correct assignments being at 40.77 and 39.34 ppm, respectively. The 2D-COSY spectrum confirmed the relative stereochemistry depicted in structure **4**, the rigid nature of the isoquinuclidine ring resulted in different chemical shifts for the geminal hydrogens on positions C-3, C-6, C-7, and C-8. The ^2H NMR of the labeled dioscorine (100 mg in 458 mg of unenriched chloroform) exhibited only two significant peaks above the natural abundance level, one at 7.26 ppm (due to natural abundance of deuterium in the chloroform) and the other at 2.36 ppm. By integration of these two peaks it was established that the ^2H enrichment at C-1 of dioscorine was 0.134%. Since the deuterium enrichment at C-6 in the administered trigonelline was 92.5%, this represents a specific incorporation of ^2H of 0.14%, in excellent agreement with the specific incorporation of ^{14}C. Trigonelline thus serves as a direct precursor of the isoquinuclidine ring of dioscorine.

Acknowledgment. This investigation was supported by research Grant GM-13246-30 from the National Institutes of Health, U.S. Public Health Service. We thank Dr. Stephen B. Philson for help in determining the NMR spectra. We are indebted to Dr. Nestor L. Pido of Visayas State College of Agriculture, Philippine Root Crop Research and Training Center, for the excellent viable specimens of *Dioscorea hispida*.

Note Added in Proof. The administration of [*methyl*]-^{14}C,2-^{2}H,^{3}H]trigonelline ($^3H/^{14}C$ = 2.77) to *Dioscorea hispida* afforded dioscorine ($^3H/^{14}C$ = 2.9, specific inc. (^{14}C): 1.6%) which was

(5) We have no explanation for the different levels of incorporation of labeled nicotinic acid into dioscorine in *Dioscorea hispida*. The production of dioscorine in this species seems to be dependent on several factors: age of plant, time of year, and temperature of cultivation. None of these factors were the same in the feeding experiments reported in Table I. In previous work[2], [2-^{14}C]nicotinic acid and [5,6-$^{13}C_2$,^{14}C]nicotinic acid were incorporated into dioscorine with absolute incorporations of 1.9% and 0.42%, respectively.

(6) Corley, D. G.; Tempesta, M. S.; Iwu, M. M. *Tetrahedron Lett*, *26*, 1615. In this article the authors inadvertently depicted dioscorine with the incorrect stereochemistry (private communication from M.S.T. and A. R. Pinder).

(7) Prepared as previously described: Späth, E.; Bobenberger, G. *Ber.* **1944**, *77*, 362, by reaction of [6-^{2}H,^{3}H]nicotinic acid with [^{14}C]methyl iodide followed by treatment of the resultant 3-carboxy-*N*-methylpyridinium iodide with silver hydroxide.

enriched with deuterium only at the 3-*pro-R* position (the 3a-H closest to the lactone ring), indicative of a stereospecific reduction in the biosynthesis of the alkaloid from trigonelline.

Supplementary Material Available: 2D-HETCOR and 2D-COSY of natural dioscorine, with ^{13}C, ^{1}H chemical shifts and $^{1}H-^{1}H$ couplings; ^{2}H NMR spectrum of enriched dioscorine (5 pages). Ordering information is given on any current masthead page. These data will be provided with requests for reprints.

Crown Thioether Chemistry. Synthesis and Structure of [Bis(1,4,7-trithiacyclononane)rhodium] Tris(triflate): Stabilization of Monomeric Rh(II)

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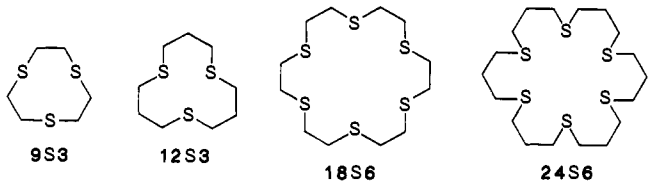
In contrast to the extensive coordination chemistry of Co(II), monomeric Rh(II) complexes have proven elusive by virtue of their propensity for dimerization (e.g., $Rh_2(OAc)_4$) and/or disproportionation to Rh(III) and Rh(I).[1] Recently we have been exploring the coordination chemistry of crown thioethers[2] such as 9S3,[3,4] 18S6,[3-6] and 24S6[7] with a view toward stabilization of



low oxidation and spin states, in the expectation that the unusual electronic structures induced by these ligands would confer unusual reactivity as well. Thioether complexes of rhodium attract particular interest owing to their potential parallel to industrially important rhodium phosphine complexes. We report herein our synthetic, physical, and structural investigation of $[Rh(9S3)_2]^{3+}$, the first reported homoleptic thioether complex of Rh(III), and its reduction to a rare example of a stable monomeric Rh(II) complex.[1]

Reaction of rhodium(III) triflate (prepared by reaction of $RhCl_3 \cdot 3H_2O$ with silver triflate) with 2 equiv of 9S3[3] in MeOH gives a pale orange solution that upon concentration and cooling deposits colorless needles (yield: 48%). Anal. Calcd for $RhC_{15}H_{24}S_9F_9O_9$: C, 19.78; H, 2.66; found (Oxford microanalytical service) C, 19.44; H, 2.58. ^{1}H NMR (300 MHz, CD_3CN, TMS, δ) 3.52 (m) at room temperature. Recrystallization from MeOH gave crystals suitable for X-ray diffraction measurements.[8]

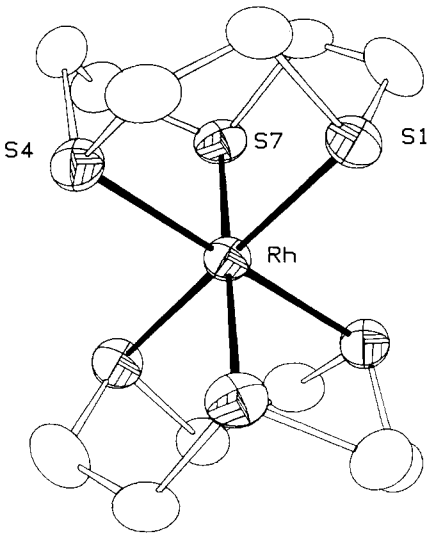


Figure 1. ORTEP drawing of $[Rh(9S3)_2]^{3+}$ cation showing thermal ellipsoids at 50% probability level (hydrogen atoms are omitted for clarity). Atomic numbering of the unique 9S3 ring follows IUPAC nomenclature (i.e., S1, C2, C3, S4, etc.).

The molecular structure of $[Rh(9S3)_2]^{3+}$ (Figure 1) shows a rigorously centrosymmetric RhS_6 coordination sphere in which the metal ion nestles between two 9S3 rings. Two of the unique Rh–S distances are somewhat longer (2.345 (3) and 2.348 (3) Å) than the third (2.331 (2) Å); similar Rh–S bond lengths have been reported for a dimethyl sulfide complex of Rh(III).[9] Interestingly, these distances closely approach those very recently found for $[Ru(9S3)_2]^{2+}$ (in which Ru–S distances range from 2.331 (1) to 2.344 (1) Å),[10] despite the difference in charge between the two complexes. Intraligand dimensions and torsional angles differ insignificantly from those found either in other complexes of this ligand[10,11] or, indeed, in the free ligand itself.[12]

Electrochemical studies of $[Rh(9S3)_2]^{3+}$ reveal an extraordinary result. Cyclic voltammetry in $MeNO_2$ on a glassy carbon electrode (Figure 2) shows *two quasi-reversible one-electron processes* at −309 and −721 mV versus SCE (ΔE_{pp} = −71 and −98 mV, respectively; ν = 50 mV/s). Controlled potential coulometry establishes that both processes entail transfer of one-electron (n = 1.05 and 0.97, respectively). Preparative electrolysis at −500 mV affords a straw-colored solution that exhibits an EPR spectrum (at 298 K) with g = 2.046 without resolved ^{103}Rh (I = 1/2, 100%)

† Inorganic Chemistry Laboratory.

(1) For rare examples of monomeric Rh(II) complexes, see: Bennett, M. A.; Bramley, R.; Longstaff, P. A. *J. Chem. Soc., Chem. Commun.* **1966**, 806. Billig, E.; Shupack, S. I.; Water, J. H.; Williams, R.; Gray, H. B. *J. Am. Chem. Soc.* **1964**, *86*, 926.

(2) The following abbrevations are used: 9S3, trithia-9-crown-3, 1,4,7-trithiacyclononane; 18S6, hexathia-18-crown-6, 1,4,7,10,13,16-hexathiacyclooctadecane; 24S6, hexathia-24-crown-6, 1,5,9,13,17,21-hexathiacyclotetracosane.

(3) Hartman, J. R.; Cooper, S. R. *J. Am. Chem. Soc.* **1986**, *108*, 1202.

(4) Hartman, J. R.; Hintsa, E. J.; Cooper S. R. *J. Am. Chem. Soc.* **1986**, *108*, 1208.

(5) Hartman, J. R.; Hintsa, E. J.; Cooper S. R. *J. Chem. Soc., Chem. Commun.* **1984**, 386.

(6) Hintsa, E. J.; Hartman, J. R.; Cooper, S. R. *J. Am. Chem. Soc.* **1983**, *105*, 3738.

(7) Rawle, S. C.; Hartman, J. R.; Watkin, D. J.; Cooper, S. R.; *J. Chem. Soc., Chem. Commun.* **1986**, 1083.

(8) Crystal data: $RhC_{15}H_{24}S_9F_9O_9$, fw = 910.83, monoclinic, space group $C2/c$ (no. 15), a = 18.638 (6) Å, b = 10.643 (3) Å, c = 16.075 (2) Å, β = 105.93 (2)°, V = 3066.1 Å^3, Z = 4, d_{calcd} = 1.97 g/cc. A crystal (0.1 mm × 0.1 mm × 0.4 mm) was sealed in an X-ray capillary for crystallographic studies. An Enraf Nonius CAD4 diffractometer with Cu Kα radiation (1.5418 Å) was used for collection of 4021 data with $2\theta \leq 140°$. The 1547 reflections with $I > 3\sigma(I)$ remaining after data reduction and averaging of equivalent reflections were used in subsequent calculations. Three standard reflections that were measured every hour showed no decay. Calculations were performed with the CRYSTALS crystallographic programs on a VAX 11/750 computer, with atomic scattering factors from the usual source. An empirical absorption correction was applied. The Rh atom was found from a three-dimensional Patterson map, and the remaining non-hydrogen atoms were found by Fourier syntheses. Approximately half of the hydrogen atoms were also found; all hydrogen atoms were included at calculated positions, and a group isotropic thermal parameter was refined. Full-matrix least-squares refinement converged to R = 6.84% (R_w = 8.65%) for 199 parameters. One of the triflate groups is disordered across a twofold axis; it was refined as two molecules each with half occupancy. The highest peak in the final difference map was 1.3 e/Å^{-3} and was found next to the disordered triflate.

(9) Sokol, V. I.; Nikoleav, V. N.; Porai-Koshits, M. A.; Kochetkova, A. P.; Sveshnikova, L. B. *Koord. Khim.* **1975**, *1*, 675.

(10) Rawle, S. C.; Cooper, S. R. *J. Chem. Soc., Chem. Commun.* **1987**, 308.

(11) Setzer, W. N.; Ogle, C. A.; Wilson, G. S.; Glass, R. S. *Inorg. Chem.* **1983**, *22*, 266.

(12) Glass, R. S.; Wilson, G. S.; Setzer, W. N. *J. Am. Chem. Soc.* **1980**, *102*, 5068.

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