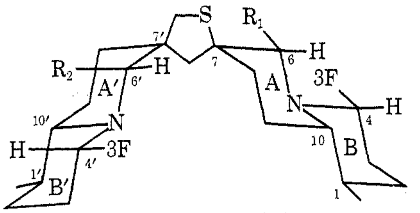
See Editorial, *J. Org. Chem.*, **38**, No. 19, 4A (1972)

Absolute Configuration of C_{30}, Sulfur-Containing Nuphar Alkaloids Determined by Circular Dichroism[1]

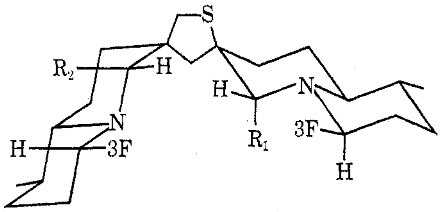
Summary: The circular dichroism resulting from an α-thioimmonium ion function was studied in 6-hydroxythiobinupharidine, 6,6′-dihydroxythiobinupharidine, and 6,6′-dihydroxythionuphlutine B to determine the absolute stereochemistry of thiobinupharidine and thionuphlutine B.

Sir: We have recently reported in detail the evidence for the relative stereochemistry of the C_{30}, sulfur-containing alkaloids thiobinupharidine (**1**) and thionuphlutine B (**2**).[2] An appreciation of the influence of sulfur–immonium ion interaction was instrumental in arriving at these structures. Manifestations of the interaction were (1) the demonstrated stereospecificity of the deuteride reduction of the bishemiaminals **3** and **4** to **1** and **2**, respectively, and (2) the appearance of the acid-induced bands in the 290–300-nm region of the uv of **3** and **4** as well as the naturally occurring monohemiaminal **5** and the model compounds **6** and **7**.

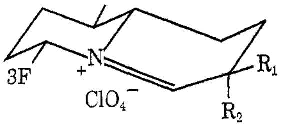
Measurement[3] in 95% ethanol of the CD of the immonium perchlorates derived from the hemiaminals mentioned above provides data which allow the assignment of the absolute configuration to these C_{30} alkaloids.

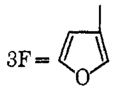


1, $R_1 = R_2 = H(D)$
3, $R_1 = R_2 = OH$
5, $R_1 = OH; R_2 = H$



2, $R_1 = R_2 = H(D)$
4, $R_1 = R_2 = OH$





6, $R_1 = SCH_3; R_2 = CH_3$
7, $R_1 = CH_3; R_2 = SCH_3$
8, $R_1 = OH; R_2 = CH_3$

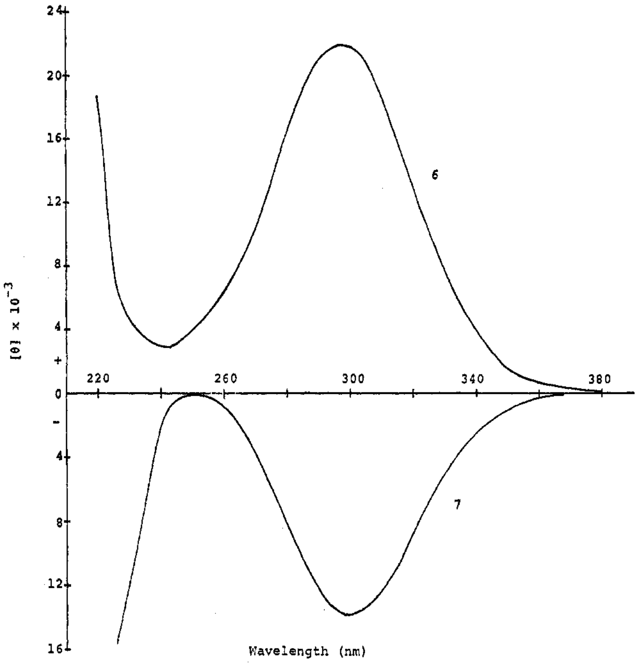


Figure 1.—The circular dichroism of immonium perchlorates derived from 7β-methylthiodeoxynupharidin-6α-ol (**6**) and 7α-methylthiodeoxynupharidin-6β-ol (**7**).

Thus the pseudoenantiomeric pair of perchlorates **6** and **7** give, respectively, positive ($[\theta]^{25}_{298}$ 22,000, *c* 1.5 mg/10 ml) and negative ($[\theta]^{25}_{300}$ −14,000, *c* 0.8 mg/5 ml) CD bands as shown in Figure 1. The relative configuration of the C_7 sulfur atom in **6** and in the immonium ions derived from **3** and **5** is the same. On the other hand, the relative configuration of the sulfur atom in **7** and in the immonium ion from **4** is the same but different from that of **3**, **5**, and **6**.[2] Since **6** and **7** are derived from (−)-deoxynupharidine whose absolute configuration has been established[4,5] (1*R*,4*S*,7*S*,10*S*), the set of curves given in Figure 1 can be used as comparison standards for ascertaining the absolute stereochemistry of other α-thioimmonium ions of the nuphar alkaloid series. Significantly the immonium ion **8** also gives a positive CD band ($[\theta]^{25}_{230}$ 8800) but at a much lower wavelength, a result consistent with the report that simple immonium ions absorb in the uv in the 220–230-nm region[6] and our earlier observation that interaction of sulfur with an immonium ion is necessary for the appearance of the longer wavelength absorption in the 300-nm region.[2]

As the curves of Figure 2 show, perchlorates derived from bishemiaminal **3** and monohemiaminal **5** give

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[1] Support of this work by the National Institutes of Health, U. S. Public Health Service (Grant No. AI10188) is gratefully acknowledged.

[2] R. T. LaLonde, C. F. Wong, and K. C. Das, *J. Amer. Chem. Soc.*, in press.

[3] CD measurements were performed on a Jasco Model 5 spectropolarimeter at the concentrations indicated.

[4] (a) C. F. Wong, E. Auer, and R. T. LaLonde, *J. Org. Chem.*, **35**, 517 (1970); (b) I. Kawasaki, I. Kusumoto, and T. Kaneko, *Bull. Chem. Soc. Jap.*, **41**, 1264 (1968); (c) K. Oda and H. Koyama, *J. Chem. Soc. B*, 1450 (1970).

[5] (−)-Deoxynuphridine gives a negative plain curve in the 310–230-nm region.

[6] G. Opitz, H. Hellmann, and H. W. Schubert, *Justus Liebigs Ann. Chem.*, **623**, 117 (1959).

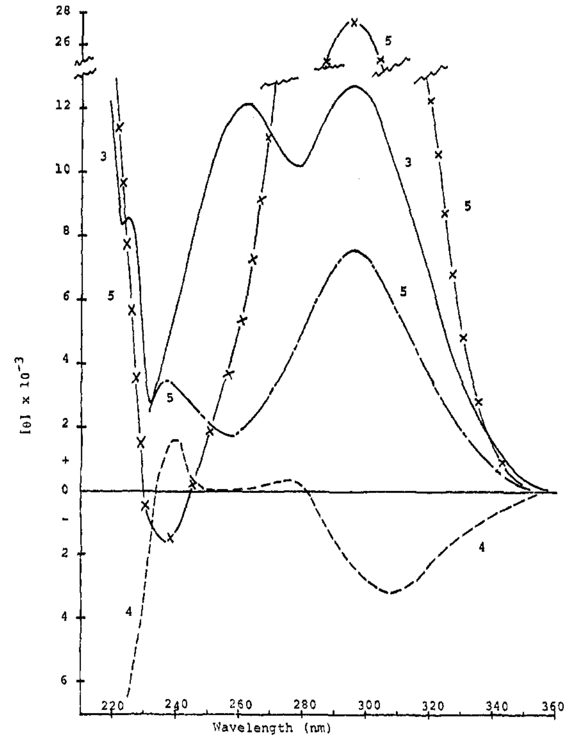

Figure 2.—The circular dichroism of immonium perchlorates derived from 6,6′-dihydroxythiobinupharidine (**3**) (—); 6,6′-dihydroxythionuphlutine B (**4**) (- - -); 6-hydroxythiobinupharidine (**5**) (- - -, in neutral EtOH), (- × -, in EtOH with added perchloric acid).

positive CD bands ($[\theta]^{25}_{296}$ 13,000, c 3.5 mg/5 ml and $[\theta]^{25}_{296}$ 7800, c 1.3 mg/1 ml, respectively), whereas the perchlorate of bishemiaminal **4** gives a negative CD band ($[\theta]^{25}_{308}$ −3200, c 1 mg/2 ml). Therefore, since the relative configurations of carbons 1, 4, and 10 in the C_{30} alkaloids and in (−)-deoxynupharidine were demonstrated to be the same but the configuration at C-7 to be variable,[2] the absolute configurations of chiral centers in the AB quinolizidine system of the C_{30} alkaloids are now known and are represented in the structures given. Reasonably the configurations of corresponding centers in AB and A′B′ quinolizidine ring systems would be the same judging from the near symmetrical (C_2) incorporation of two deoxynupharidine moieties into the C_{30} skeleton. However, this latter proposal is being checked experimentally by studies now in progress.

The appearance of positive CD bands at 275 nm for the perchlorate of **4** and at 265 nm for the perchlorate of **3** results from an A′B′ immonium ion. The CD bands in the 230–240-nm region evident in the CD of perchlorates of **4** and **5** possibly are due to the presence of α-ethoxyamines which are in equilibrium with immonium ions. These CD bands become more intense in dilute solution but disappear altogether, with simultaneous enhancement of the immonium ion bands, when several drops of perchloric acid are added. This is demonstrated in the case of **5** by the CD curve in Figure 2.

These results demonstrate that the CD of immonium ions holds considerable promise as a simple method for gaining stereochemical information. Since many immonium ions are naturally occurring in the form of hemiaminals and are readily available by oxidation of tertiary amines, the CD of immonium ions would appear to have special applicability to the study of alkaloid structure.

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RECEIVED MAY 9, 1973

Reversible Deuteration of 2,6-Dimethoxy-1,4-benzoquinone in Alkali

Summary: Base catalyzes rapid replacement by deuterium of the ring protons in 2,6-dimethoxy-1,4-benzoquinone in D_2O, establishing that nucleophilic addition of a hydroxyl ion to form an *o*-quinal structure is the primary step in alkaline decomposition of the quinone.

Sir: On treatment with alkali, quinones undergo rapid decomposition and polymerization to yield dark pigments of humus-like character.[1] Quinone percursors of humins arise in nature as fungal metabolites[2] or as products of biodegradation of plant lignins by fungal phenol oxidases.[3] One of the quinones frequently encountered as a product of fungal or enzymatic degradation of lignin[3] or lignin model compounds[3-5] is 2,6-dimethoxy-1,4-benzoquinone (**1**). This compound and its conversion products are therefore considered to be likely components of soil humus.

The rate of decomposition of unsubstituted *p*-benzoquinone in 0.1 N sodium hydroxide is so fast that special flow methods had to be applied in efforts to study the kinetics and course of the primary reaction.[6] However, the dimethoxy-*p*-benzoquinone (**1**) is relatively stable in alkali, where it undergoes unusual base-catalyzed exchange reactions which indicate that a nucleophilic addition of a hydroxyl ion onto the quinone must be the initial step in its alkaline decomposition.

The quinone **1** was prepared by nitric acid oxidation of 2,6-dimethoxyphenol[5] and purified by vacuum sublimation (mp 255°). Addition of alkali to a yellow aqueous solution of **1** [λ_{max} 289, 396 nm (ϵ 14,500, 660)] produced a colorless solution with only a single maximum at 249 nm (ϵ 15,300). On immediate reacidification, the original spectrum was regenerated and unchanged **1** could be recovered almost quantitatively from the solution by extraction with chloroform [λ_{max} (in $CHCl_3$) 286, 376 nm (ϵ 18,000, 600)].

A sample of **1** [pmr in $CDCl_3$, δ 3.82 (s, 2,6-OCH_3), 5.85 (s, 3,5-H)] was dissolved in alkaline D_2O and the solution acidified 1 min later with HCl in D_2O. The

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(1) H. Erdtman and W. Stjernstrom, *Chem. Ind.* (*London*), 1599 (1960); W. Flaig, *et al.*, *Chem. Geol.*, **3**, 161 (1968); *Naturwiss.*, **47**, 516 (1960); *Justus Leibigs Ann. Chem.*, **597**, 196 (1955).

(2) K. Haider and J. P. Martin, *Soil Biol. Biochem.*, **2**, 145 (1970); *Soil Sci.*, **107**, 260 (1969); *Soil Sci. Soc. Amer. Proc.*, **31**, 766 (1967).

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(6) M. Eigen and P. M. Matthies, *Chem. Ber.*, **94**, 3309 (1961).