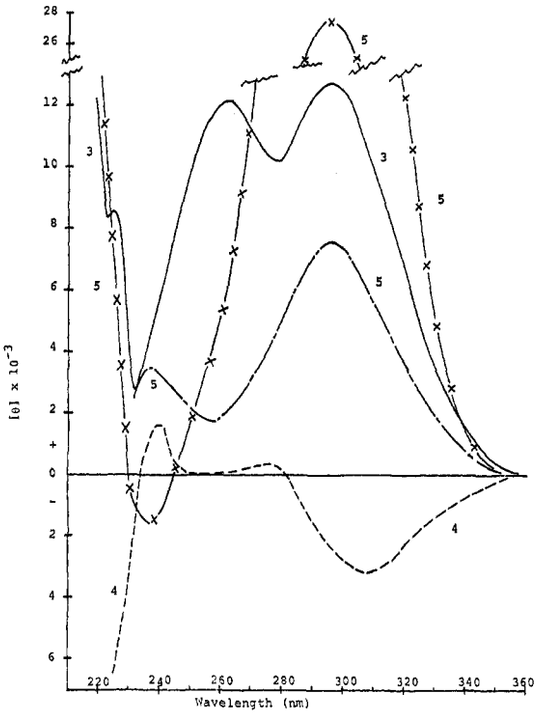

Figure 2.—The circular dichroism of immonium perchlorates derived from 6,6′-dihydroxythiobinupharidine (**3**) (—); 6,6′-dihydroxythionuphlutine B (**4**) (- - -); 6-hydroxythiobinupharidine (**5**) (- - -, in neutral EtOH), (- × -, in EtOH with added perchloric acid).

positive CD bands ($[\theta]_{296}^{25}$ 13,000, *c* 3.5 mg/5 ml and $[\theta]_{296}^{25}$ 7800, *c* 1.3 mg/1 ml, respectively), whereas the perchlorate of bishemiaminal **4** gives a negative CD band ($[\theta]_{308}^{25}$ −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.

DEPARTMENT OF CHEMISTRY
STATE UNIVERSITY OF NEW YORK
COLLEGE OF ENVIRONMENTAL SCIENCE AND FORESTRY
SYRACUSE, NEW YORK 13210

C. F. WONG
ROBERT T. LALONDE*

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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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(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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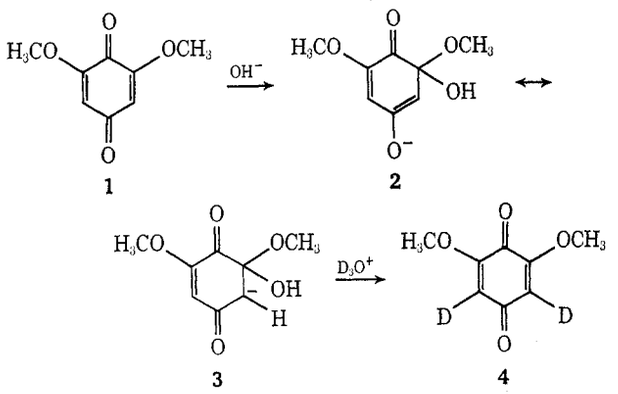
(5) W. Baker, *J. Chem. Soc.*, 622 (1941).

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

solution was extracted with chloroform, the extract dried, and the solvent removed. The pmr of the residue in $CDCl_3$ showed only a singlet at δ 3.82, indicating that the recovered product was 3,5-dideuterio-2,6-dimethoxy-1,4-benzoquinone (**4**).

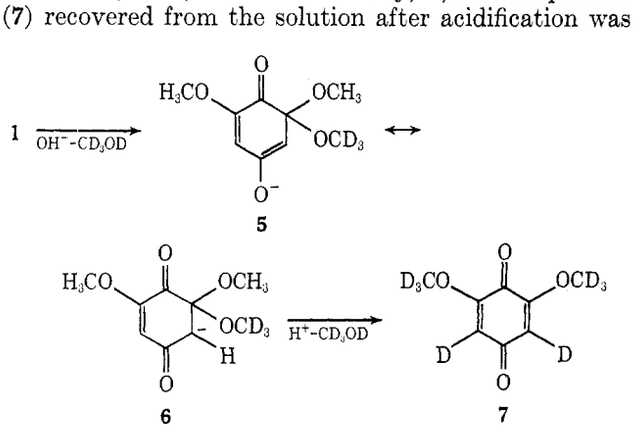
The formation of **4** can be explained as follows. In



alkaline solution, a hydroxyl ion adds on to **1** to yield an anion hitherto formulated as **2**;[4b,c,6] however, this is evidently tautomeric with the anion **3**, a form through which exchange of the ring protons can occur readily in D_2O *via* deuteration and deprotonation. Reacidification in D_2O therefore yields **4**. The original quinone **1** was re-formed from **4** by dissolution in NaOH–H_2O and acidification with HCl–H_2O. This rapid reversible deuteration therefore indicates the immediate formation in base of adducts of the type **2** ↔ **3**, which has been postulated as the first step in the alkaline decomposition of quinones.[4b,c,6]

Even for a substituted quinone, **1** is atypical in its relative stability in base. Its decomposition in alkali, as measured by the decay of the peak at 289 nm after reacidification, follows first-order kinetics with a half-life of 30 min at pH 10.5 and 20°. Other substituted quinones (1,2- and 1,4-naphthoquinone, 2-methyl-1,4-naphthoquinone, 2-methoxy-, 2,5-dimethyl-, 2,6-dimethyl-, 2,5-dichloro-, and 2,6-dichloro-1,4-benzoquinone, and 3,5-dimethoxy-1,2-benzoquinone) all decomposed within 1 min at pH 10.5. Regeneration of original quinones by acidification could not be established by uv or pmr spectroscopy. It was, therefore, impossible to establish deuterium exchange in alkaline solution.

On treatment of **1** with NaOH or CD_3ONa in CDCl–CD_3OD, both the methoxyl and proton resonances were immediately discharged from the pmr spectrum. 3,5-Dideuterio-2,6-bis(trideuteriomethoxy)-1,4-benzoquinone (**7**) recovered from the solution after acidification was



reconverted to **1** with NaOH in CH_3OH followed by acidification.

The exchange of the methoxyl probably involves an intermediate quinal (quinol ether) adduct (**6** ↔ **7**) analogous to the *o*-hemiquinal structure (**2** ↔ **3**). Rapid exchange of the methoxyl groups in **1** in alkaline solution by other alkoxyl groups has also been demonstrated by pmr and esr.[4c]

USDA–FS FOREST PRODUCTS LABORATORY
MADISON, WISCONSIN 53705
JOHN R. OBST*
JOHN M. HARKIN

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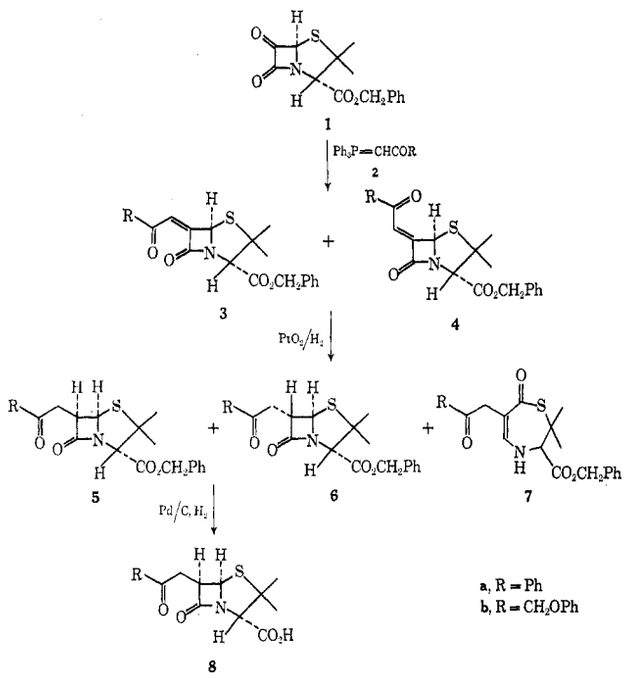
Benzyl 6-Oxopenicillanate and Derivatives. II

Summary: The amide side chain of a penicillin has been removed and the carbon analogs of penicillin V and phenylpenicillin have been synthesized stereospecifically; the penicillin V analog has antibiotic activity and penicillinase resistance.

Sir: We have reported[1] the preparation of 6β-phenoxyacetoxypenicillanic acid—a 6-oxygen analog of penicillin V, from benzyl 6-oxopenicillanate (**1**). This versatile



intermediate can also be transformed to 6β-phenoxyacetylmethylpenicillanic acid (**8b**)—a 6-carbon analog of penicillin V. Surprisingly, this relatively major change in structure resulted in a compound still containing appreciable antibiotic activity. In addition, **8b** was resistant to *Bacillus cereus* penicillinase.[2]

As a model side-chain precursor, the readily available benzoylmethylenetriphenylphosphorane (**2a**) was allowed to react with benzyl 6-oxopenicillanate (**1**) in refluxing benzene to give, after column chromatography, a yellow oily product (64%), benzyl benzoylmethylene-

(1) Y. S. Lo and J. C. Sheehan, *J. Amer. Chem. Soc.*, **94**, 8253 (1972).

(2) Bristol Laboratories, Division of Bristol-Myers Co., Syracuse, N. Y. In the previous communication,[1] crude 6β-phenoxyacetoxypenicillanic acid was reported to be inactive. The potassium salt of this acid has since been retested and showed some antibacterial activity. Presumably the crude acid sample had decomposed before bioassay.