thermometric titration study of adenine, ribose, adenosine, 2′-deoxyadenosine, 3′-deoxyadenosine, and 2′-O-methyladenosine which conclusively shows the acidity of adenosine to be associated with the presence of both the 2′- and 3′-OH groups and that substitution of H for either the 2′- or 3′-OH group or OCH_3 for the 2′-OH group results in loss of this acidity. In addition pK, $\Delta H°$, and $\Delta S°$ values obtained by the entropy titration method[6] are reported for adenosine ionization.

The chemicals used were the highest purity available from California Biochemical Corp. (Grade A ribose, adenine, adenosine) and Sigma Chemical Co. (Sigma grade deoxyadenosine) or were synthesized (2′-O-methyladenosine, 3′-deoxyadenosine).[7]

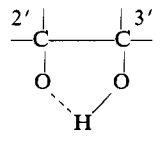
In Figure 1 are plotted thermometric titration data taken from thermograms obtained by titration with 0.6 F NaOH solution of 0.01 F solutions of adenosine, ribose, 2′-deoxyadenosine, sodium adenate ($NaC_5H_4N_5$), 0.002 F 2′-O-methyladenosine, and 0.004 F 3′-deoxyadenosine. The thermograms were obtained using a precision thermometric titration calorimeter.[6,8]

The observed temperature increase (Figure 1) during the titration of 3′-deoxyadenosine, 2′-O-methyladenosine, and 2′-deoxyadenosine is quantitatively accounted for by the heat of dilution of the titrant and heat from stirring. The small differences observed among the individual curves for these substances are quantitatively accounted for by small changes between determinations in the rate of heat input from stirring. The curve for sodium adenate shows a relatively large initial increase due to the reaction of a small amount of the hydrolyzed adenate species (adenine pK = 9.8).

Calculations indicate that under the conditions used in this study proton ionization is detectable provided the pK is less than ~13.5.

The curve for ribose shows the presence of an acid–base reaction but the data have not yet been treated quantitatively. The curve for adenosine has been analyzed quantitatively,[6] assuming one dissociable proton, to obtain, at zero ionic strength and 25°, pK = 12.35 ± 0.03, $\Delta H°$ = 9.7 ± 0.1 kcal./mole, and $\Delta S°$ = −23.9 ± 0.3 e.u. for the reaction adenosine → adenosine$^-$ + H^+. This pK value is in good agreement with that reported by Levene, *et al.*[1] (12.5).

The curves for sodium adenate and ribose clearly show that the proton in adenosine is ionized from the ribose moiety. Further, the fact that substitution of CH_3 for H on the 2′-hydroxyl or substitution of H for OH in either the 2′- or 3′-position in adenosine causes a loss of acidity indicates that the two adjacent hydroxyl groups are a necessary structural feature for that acidic character to exist. Two possible explanations for this are (1) the combined inductive effect of the vicinal 2′- and 3′-hydroxyl groups and/or (2) the anion is stabilized by a hydrogen-bonded ring; *e.g.*



(6) L. D. Hansen, J. J. Christensen, and R. M. Izatt, *Chem. Commun.* (London), **3**, 36, 1965.

(7) The authors greatly appreciate the loan of 50 mg. of 2′-O-methyladenosine and 100 mg. of 3′-deoxyadenosine by Dr. Roland K. Robins for use in this study.

(8) J. J. Christensen, L. D. Hansen, and R. M. Izatt, *Rev. Sci. Instr.*, in press.

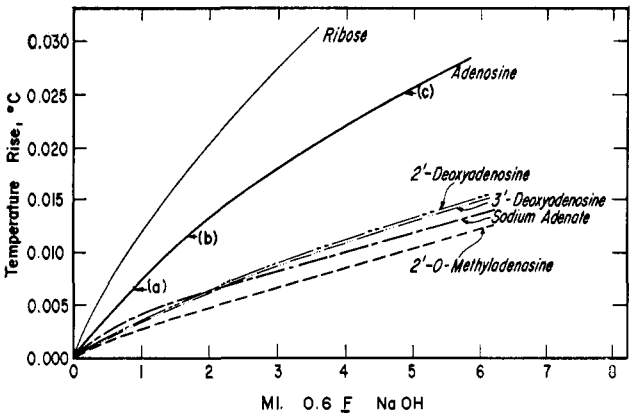


Figure 1. Actual thermometric titration curves for titration of aqueous solutions of the indicated compounds with 0.6 F NaOH. Temperature 25°; initial volume in calorimeter 100 ml; pH of adenosine solution 11.6 (a), 12.0 (b), and 12.5 (c).

It would now be of interest to determine whether 3′-O-methyladenosine is acidic; however, this compound is not yet available for study.

The data presented here suggest that the known acidity[1,9] of the ribose in RNA is a result of the combined effect of the 2′- and 3′-hydroxyl groups. Substitution of H for OH in the 2′-position (DNA) should result in loss of this acidity. Since the known chemical reactivity of the 2′- and 3′-positions in these substances would be expected to parallel the acidity of the OH groups, the different biological functions of DNA and RNA may be closely related to these acidity differences.

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(10) (a) To whom inquiries should be directed. (b) National Defense Education Act Predoctoral Fellow.

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Absolute Configurations of Sulfoxides by Asymmetric Oxidation of Sulfides[1]

Sir:

The oxidation of nondissymmetric sulfides by dissymmetric oxidizing agents leads to optically active sulfoxides,[2,3] generally in low optical yields.[4] It has been

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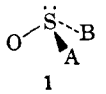
Table I. Specific Rotations of Some Alkyl Benzyl Sulfoxides in Ethanol and Chloroform

Alkyl group	In ethanol: Percamphoric acid oxidn.,[a] deg.	In ethanol: Grignard synthesis,[b] deg.	In chloroform: Percamphoric acid oxidn.,[a] deg.	In chloroform: Grignard synthesis,[b] deg.
Methyl[c]	+1.0 (1.0)	+96	−0.5 (0.9)	−55
Ethyl	+1.2 (2.5)	+47	−2.9 (3.0)	−97
n-Butyl	+0.7 (4.4)	+16	−1.8 (1.7)	−105
Isopropyl	+5.3 (4.5)	+119	+0.6 (20)	+3
t-Butyl	+12.0 (4.3)	+281	+10.3 (4.3)	+240

[a] With the exception of the methyl compound, the data are taken from ref. 2. Values in parentheses are *maximum* per cent optical purities calculated on the basis of the rotations listed in the adjoining column. [b] Reaction of alkylmagnesium halide and I. [c] Present work, following the procedure reported in ref. 2.

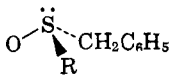
suggested[2] on the basis of a proposed transition state that the direction of asymmetric synthesis follows a general pattern which can be summarized as follows: oxidation of a sulfide A–S–B with (+)-monopercamphoric acid gives a preponderance of the enantiomer shown in stereoformula **1** when A is bulkier than B.



1

Although this generalization correctly predicted the absolute configurations of alkyl phenyl sulfoxides,[4] we now wish to report that it breaks down in the case of alkyl benzyl sulfoxides and thus may not be used as a general scheme for the assignment of absolute configurations to sulfoxides.

Reaction of phenylmethanesulfinyl chloride ($C_6H_5CH_2SOCl$) with *l*-menthol followed by fractional crystallization of the reaction mixture afforded a diastereomer (I) of *l*-menthyl phenylmethanesulfinate, $[\alpha]_D$ +105° (chloroform). Reaction of I with *p*-tolylmagnesium bromide gave benzyl *p*-tolyl sulfoxide (II), $[\alpha]_D$ +228° (acetone), 91% optically pure based on the highest reported rotation.[5] The absolute configuration of II is (*R*),[4,5] corresponding to stereoformula **2**, and since the Grignard reaction proceeds with inversion of configuration,[4,6] it follows that ester I has the (*R*) configuration at sulfur.[7] Reaction of a variety of branched and unbranched alkylmagnesium halides with I gave the compounds listed in Table I, all of which must have the configuration shown in stereoformula **2**.



2

R = alkyl or *p*-tolyl

The rotational signs of the sulfoxides derived from I agree with the signs of the sulfoxides obtained by (+)-percamphoric acid oxidation of the corresponding sulfides (Table I). Therefore the predominant enantiomers produced in the asymmetric oxidation also have configuration **2**. It follows that while the configurational assignments[2] based on the proposed transition state are correct in the cases of isopropyl benzyl and *t*-butyl benzyl sulfoxides, they are incorrect in the cases of *n*-alkyl benzyl sulfoxides (and, by extension, methyl benzyl sulfoxide) since the benzyl group is judged to be bulkier than *n*-alkyl groups.[2]

The stereospecificities of the asymmetric oxidations are extremely low. Quantitative comparisons are rendered suspect by inconsistencies in the optical yields as measured in ethanol and chloroform (Table I); these discrepancies are most likely due to inaccuracies in the small rotations observed in the asymmetric oxidations.[2] We therefore refrain from rationalization of our findings at this time.

A detailed study of this and related asymmetric oxidations is now under way. We shall report separately on the optical rotatory dispersion (including solvent effects) of alkyl benzyl sulfoxides.

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Circular Dichroism of Copper(II) Complexes with Optically Active Amino Acids

Sir:

Pfeiffer and Christeleit[1] have reported the usefulness of optical rotatory dispersion (ORD) of bis(optically active amino acid)copper(II) complexes as a tool in determining the configurations of the amino acids. The copper(II) complex of an L-amino acid shows a negative Cotton effect in the region of the visible d → d absorption band, and the complex of a D-amino acid a positive Cotton effect. The present communication reports a circular dichroism (CD) study of the complexes $[Cu(am)_2]$ in aqueous solutions (am = L- and D-alanine, L-serine, L-valine, L-threonine, L-allothreonine, L-proline, and L-hydroxyproline). The CD curves in the region from 1000 to 400 mμ were obtained on a Shimadzu spectrophotometer with CD attachment using 0.025 *M*, 0.05 *M*, or saturated solutions of those complexes in a 1-cm. cell. The copper(II) complexes employed were prepared from copper(II) hydroxide by the modified method of Abderhalden and Schnitzler.[2]

As might have been expected from recent CD studies by other workers[3,4] the split components of the d → d transition were clearly separated. The CD curve of $[Cu(L\text{-ala})_2]$ shows a small positive band at about 730 mμ and two negative bands at 630 and 565 mμ (Figure 1). The curve of $[Cu(L\text{-ser})_2]$ is similar to that of $[Cu(L\text{-ala})_2]$ on the whole, namely, a small positive peak at about 730 mμ, a negative band at 595 mμ, and a negative shoulder at about 640 mμ. However, another small

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