Wilke, *Tetrahedron Lett.*, 1457 (1972); (d) for an early review, see G. Wilke, *Angew. Chem., Int. Ed. Engl.*, **2**, 105 (1963).

(2) (a) P. Heimbach and H. Hey, *Angew. Chem., Int. Ed. Engl.*, **9**, 528 (1970); (b) P. Heimbach and W. Brenner, *ibid.*, **6**, 800 (1967); (c) for reviews, see H. Buchholz, P. Heimbach, H. Hey, H. Selbeck, and W. Wiese, *Coord. Chem. Rev.*, **8**, 129 (1972); and P. Heimbach, *Angew. Chem., Int. Ed. Engl.*, **12**, 975 (1973).

(3) F. D. Mango, *Coord. Chem. Rev.*, **15**, 109 (1975).

(4) P. Heimbach and R. Traunmüller, "Chemie der Metall-Olefin Komplexe", Verlag Chemie, Weinheim/Bergstr., Germany, 1970.

(5) In this discussion we shall use anti and syn to describe the *relative* disposition of the two allyl units in these bis allyl complexes. To avoid confusion we shall use cis and trans to describe the geometry of an individual allyl unit.

(6) For representative allyl structures, see R. Uttech and H. Dietrich, *Z. Kristallogr., Kristallgeom., Kristallphys., Kristallchem.*, **122**, 60 (1965).

(7) G. E. Coates, M. L. H. Green, and K. Wade, "Organometallic Compounds. Volume Two, The Transition Elements", Methuen, London, 1968, p 39.

(8) (a) L. M. Stephenson, R. V. Gemmer, and J. I. Brauman, *J. Am. Chem. Soc.*, **94**, 8620 (1972); (b) L. M. Stephenson, R. V. Gemmer, and S. Current, *ibid.*, **97**, 5909 (1975).

(9) For convenience we have shown all of the species (except **10** and **11**) with a trans geometry about the $C_2$–$C_3$ and $C_6$–$C_7$ bonds. Obviously, formation of an internal $\sigma$-allyl (i.e., to $C_3$ or $C_6$) could lead, via $C_2$–$C_3$ or $C_6$–$C_7$ rotation, to cis species which may be sterically more favorable in some cases. In fact, x-ray and NMR data[1c] indicate that a cis-trans formulation is probably the energy minimum in this bis allyl family. None of these internal $\sigma$-allyls, or the rotations that result from them, can alter the deuterium stereochemistry. This is illustrated in the conversion of **6** to 1,5-cyclooctadiene (**11**), via the bis cis species **10**. Note that this same species could serve as a precursor to *cis*-divinylcyclobutane (**8**) with unchanged deuterium stereochemistry.

(10) G. S. Hammond and C. D. DeBoer, *J. Am. Chem. Soc.*, **86**, 899 (1964).

(11) This analysis is accomplished[12] by Raman spectroscopy, using a Spex 14018 Raman spectrometer equipped with a Spectra-Physics Argon ion laser (4880-Å excitation line). The meso anhydride shows bands at 691 and 1058 $cm^{-1}$, whereas the *dl* appears at 723 and 1100 $cm^{-1}$.

(12) For earlier methods of this analysis, see C. R. Childs, Jr., and K. Block, *J. Org. Chem.*, **26**, 1630 (1961).

(13) An approximation of this number can be obtained by recognizing that the average composition of the system is ~ 33% ÷ 2 = 16.5% trans,trans. Thus the number of crossed cycloadditions should be in the range of 2(0.165 × 0.835) = 28%.

(14) Our analysis will only distinguish the relative stereochemistry of adjacent (3,4 or 7,8) deuteriums in the cyclooctadiene. Our drawings imply that the mutual relationship of 3,7 and 4,8 deuteriums is syn, as a Cope rearrangement of **8** would require. No presently conceivable mechanism which would allow this relationship to be anti is consistent with the interconversion *cis,cis*-**1** $\rightleftharpoons$ *trans,trans*-**1**. Methods which would establish this more remote interrelationship of deuteriums are under investigation.

(15) Alfred P. Sloan Foundation Fellow.

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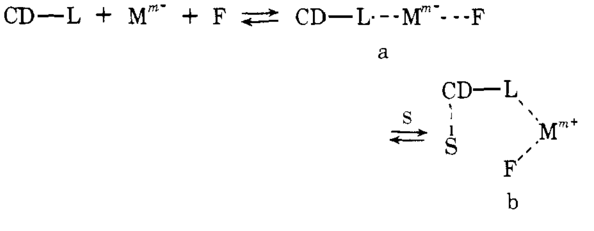
## Cyclodextrin Flexibly Capped with Metal Ion[1]

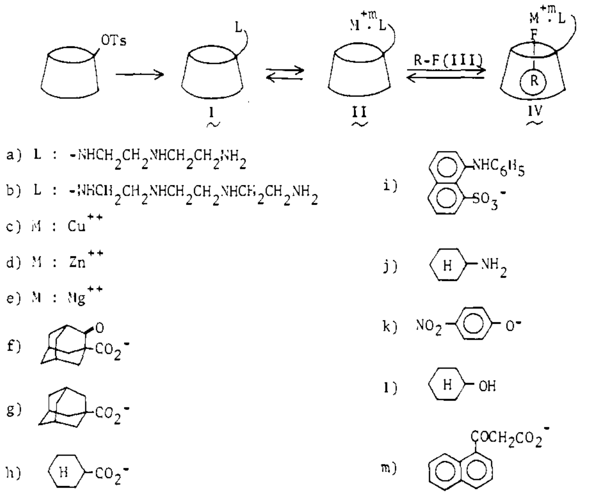
*Sir:*

Highly specific binding of substrates by hydrophobic sites of enzymes in *water* is satisfactorily modelled by artificial hosts such as parent[2] or modified[3] cyclodextrins or cyclophanes.[4] Thus, introduction of a metal ion into functionalized cyclodextrin may be an appropriate model for the studies of binding by metalloenzymes. Breslow et al.[5] reported a beautiful example of an "artificial metalloenzyme" in which a metal ion acts as a *joint* to bind the hydrophobic cavity (binding site) and the oxymate anion (catalytic site), where a substrate is bound by *single recognition* as shown by b in eq 1 as far as binding characteristics are concerned[6] (CD, cyclodextrin; $M^{m+}$, metal ion, and F, catalytic moiety; binding interactions are shown by dotted lines). The significance of metal-substrate interaction during the binding, as well as the catalytic step, is proposed for most of metalloenzymes, though not yet fully characterized in details.[7]



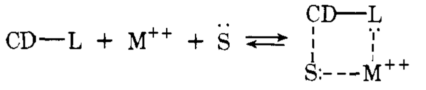
$$\mathrm{CD{-}L} + \mathrm{M}^{m+} + \mathrm{F} \rightleftharpoons \underset{\text{a}}{\mathrm{CD{-}L{\cdots}M^{m+}{\cdots}F}} \quad \xrightleftharpoons{\mathrm{S}} \quad \underset{\text{b}}{\begin{matrix} \mathrm{CD{-}L} & \\ \vdots & \cdot\,\mathrm{M}^{m+} \\ \mathrm{S} & \mathrm{F}\cdot \end{matrix}} \qquad (1)$$

We wish to report that cyclodextrins functionalized with polyamines (I) strongly interact with such metal ions as $Cu^{2+}$, $Zn^{2+}$ or $Mg^{2+}$, and the resultant cyclodextrins *flexibly* capped by metal ions (II) now can bind several anions with hydrophobic moieties (IIIf-m) much more strongly than parent or functionalized cyclodextrin I without metal coordination, as shown in Table I, providing an excellent metalloenzyme model endowed with specific metal-substrate binding interaction, a requisite for the specific catalytic function of most metalloenzyme.



(2)

Remarkably enhanced binding of hydrophobic anions by the present metallo hosts in *water* may be due to *double recognition* as schematically shown in eq 3.



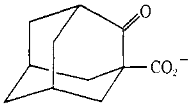
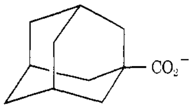
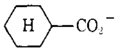
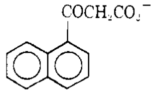
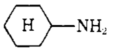
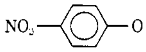
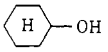
$$\mathrm{CD{-}L} + \mathrm{M}^{++} + \ddot{\mathrm{S}} \rightleftharpoons \begin{matrix} \mathrm{CD{-}L} \\ \vdots \quad\;\; \vdots \\ \ddot{\mathrm{S}}{\cdots}\mathrm{M}^{++} \end{matrix} \qquad (3)$$

Pure sample of primary tosylate of $\beta$-CD[8] was converted to $\beta$-CD functionalized with polyethylenepolyamine by treatment with the amine to be introduced at 50 °C for 5 h. Silica gel chromatography and/or Sephadex G-15 gel filtration (0.1–2 N, $NH_4OH$) gave pure cyclodextrinpolyamines I.[9] Metal binding by *apohost* I was quantitatively investigated in the case of $Cu^{2+}$ by measuring the characteristic absorption of the $Cu^{2+}$ complex at 660 and 257 nm in 0.1 N aqueous NaOH.[10] The association constant obtained from the Benesi-Hildebrand plot was $10^{17.9}$, which does not differ seriously from that of the diethylenetriamine-$Cu^{2+}$ complex, $10^{18.8}$. All of the cyclodextrinpolyamines I (*apohost*) used are desirable ligands strong enough to bind metal ion, forming *holohost* as shown in Table II. That the holohost II binds another hydrophobic ligand strongly (and specifically) was shown by the fluorescence measurements with 1-anilino-8-naphthalenesulfonate, 1,8-ANS (red shift of the fluorescence maximum and/or remarkable increase in fluorescence intensity).[4]

Dissociation constants of the ternary complex IV without chromophore or fluorophore were obtained from competition with 1,8-ANS binding. The holohost, IIa,d, binds adamantan-2-one-1-carboxylate 330 times stronger than $\beta$-CD (Table I). Such binding enhancements were seen only for the holohosts in complexing with hydrophobic anions of the types $-CO_2^-$, $-SO_3^-$, and $-O^-$, while the corresponding apohosts were only two to three times more effective than unsubstituted $\beta$-CD.

Despite no appreciable difference in the $K_d$ constant between cyclohexanol complex of holohost IIa,d and that of $\beta$-CD,

**Table I.** Dissociation Constants of Holohost-Substrate Complexes

| | Guest | Host | $K_d$, M | $K_d$ (β-CD) / $K_d$ (holohost) | |
|---|---|---|---|---|---|
| (f) |  | β-CD | $1.2 \times 10^{-3}$ | | a |
| | | Ia–$Zn^{2+}$ | $3.6 \times 10^{-6}$ | 330 | |
| (g) |  | β-CD | $4.3 \times 10^{-3}$ | | a, c |
| | | Ia–$Zn^{2+}$ | $1.9 \times 10^{-4}$ | 22.6 | |
| (h) |  | β-CD | $7.1 \times 10^{-3}$ | | a |
| | | Ia–$Zn^{2+}$ | $5.3 \times 10^{-4}$ | 13.4 | |
| (i) | 1,8-ANS | β-CD | $1.3 \times 10^{-2}$ | | b |
| | | Ib | $7.8 \times 10^{-3}$ | | |
| | | Ib–$Zn^{2+}$ | $1.9 \times 10^{-3}$ | 6.8 | |
| | | Ia–$Zn^{2+}$ | $4.5 \times 10^{-3}$ | 2.9 | |
| (m) |  | β-CD | $1.4 \times 10^{-3}$ | | a |
| | | Ia–$Zn^{2+}$ | $2.4 \times 10^{-4}$ | 5.8 | |
| (j) |  | β-CD | $2.2 \times 10^{-2}$ | | b |
| | | Ia–$Zn^{2+}$ | $4.7 \times 10^{-3}$ | 4.7 | |
| (k) |  | β-CD | $2.1 \times 10^{-3}$ | | a |
| | | Ia | $1.8 \times 10^{-3}$ | | |
| | | Ia–$Zn^{2+}$ | $8.3 \times 10^{-4}$ | 2.5 | |
| (l) |  | β-CD | $2.0 \times 10^{-3}$ | | a |
| | | Ia–$Zn^{2+}$ | $2.4 \times 10^{-3}$ | 0.83 | |

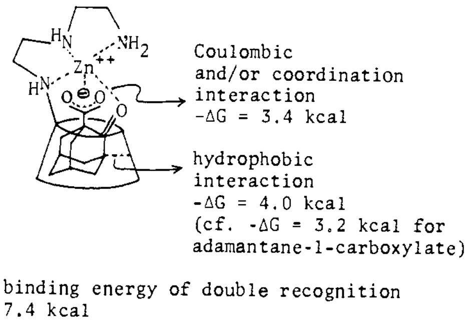
[a] In 0.05 M borate buffer (pH 10.0) at 25 °C. [b] In 0.05 M borate buffer (pH 11.0) at 25 °C. [c] Reported value, $1.60 \times 10^{-3}$ M, in a buffer of pH 9, $I = 0.2$, 0.5–0.75% (v/v) $CH_3CN$ involved (ref 6a) and $0.7 \times 10^{-3}$ M (ref 11).

**Table II.** Binding Constants of Copper Metal to Apohost I[a]

| Apohost | Metal | Log *K* | $\lambda_{max}$[b] (ε) |
|---|---|---|---|
| Ia | $Cu^{2+}$ | 17.9 | 252 (3600)<br>654 (86) |
| Diethylene-triamine | $Cu^{2+}$ | 18.8 | 247 (3800)<br>616 (74) |
| Triethylene-tetramine | $Cu^{2+}$ | 20.1 | 257 (3400)<br>652 (100) |

[a] 0.1 N NaOH, 25 °C. [b] In nm.

cyclohexanecarboxylate is bound to the zinc holohost more than 13 times stronger than to β-CD. This leads to a conclusion that in the substrate binding, metal-ligand recognition is cooperative[12] with the hydrophobic recognition by CD, and the energetics of the 'additivity' is schematically shown for IId,f in eq 4. That means highly specific binding of S is attained by



(4)

the two mutually independent specific recognition (*double recognition*), and this may provide a stepwise approach to the *multiple recognition* which is very common in biological interaction (such as drug-receptor, substrate-enzyme).

Further application of the holohosts to effective catalysis is now under way.

**Acknowledgment.** The authors are grateful to Dr. Okada and Dr. Hiyama of Osaka Municipal Technical Institute for their kind help in preparing cyclodextrins, and also to Dr. Breslow for his kind and helpful discussions.

## References and Notes

(1) Terms rigid and flexible capping are suggested by R. Breslow, private communication; see ref 3a.

(2) (a) F. Cramer, W. Saenger, and H.-Ch. Spatz, *J. Am. Chem. Soc.*, **89**, 14 (1967), and references cited therein; (b) H. J. Brass and M. L. Bender, *J. Am. Chem. Soc.*, **95**, 5391 (1973), and references cited therein.

(3) (a) J. Emert and R. Breslow, *J. Am. Chem. Soc.*, **97**, 670 (1975); (b) F. Cramer and G. Mackensen, *Angew. Chem.*, **78**, 641 (1966); (c) I. Tabushi et al., unpublished.

(4) (a) I. Tabushi, H. Sasaki, and Y. Kuroda, *J. Am. Chem. Soc.*, **98**, 5727 (1976); (b) I. Tabushi, Y. Kuroda, and Y. Kimura, *Tetrahedron Lett.*, 3727 (1976).

(5) R. Breslow and L. E. Overman, *J. Am. Chem. Soc.*, **92**, 1076 (1970).

(6) (a) A catalytic function of a metal ion of an artificial metalloenzyme was also observed: R. Breslow in "Bioinorganic Chemistry", American Chemical Society, Washington, D.C., 1971, Chapter 2; (b) Y. Chao, Ph.D. Thesis, Columbia University, 1972.

(7) (a) The function of metal in substrate binding was shown for carboxypeptidase A from the result that the nature of metal is reflected in remarkable change in $K_m$ without appreciable change in $k_{cat}$ value: D. S. Auld and B. Holmquist, *Biochemistry*, **13**, 4355 (1974). (b) J. E. Coleman in "Progress in Bioorganic Chemistry", Vol. I, E. T. Kaiser and F. J. Kézdy Ed., Wiley Interscience, New York, N.Y., 1971.

(8) Preparations of polyamine substituted β-CD's via primary monotosylate of β-cyclodextrin were presented by us at the 32nd Annual Meeting of the Chemical Society of Japan in April 1975 (preprint, III, 1301). Preparation of ethylenediamine substituted [6-deoxy-6[*N*-(2-aminoethyl)]aminocycloheptaamylose] via the primary monotosylate of β-cyclodextrin is reported (Y. Chao, ref 6b). The preparation of the primary tosylate was similar to that of the primary monotosylate of α-CD: L. D. Melton and K. N. Slessor, *Carbohyd. Res.*, **18**, 29 (1971).

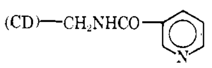
Mono-6-*O*-*p*-toluenesulfonylcycloheptaamylose: mp 160–162 °C dec; $R_f$ 0.62, silica gel (AcOEt/*i*-PrOH/$H_2O$ = 10:13:7, detection; blue spot on spraying a solution of AcOH/anisaldehyde/$H_2SO_4$/MeOH = 45:2:22:430); NMR (DMSO-$d_6$) δ 7.63 (4 H, q), 4.87 (7 H, $C_1$ H), 4.0–3.5 (42 H), 2.43 (3

H, $CH_3$). Anal. Calcd (monotosylate): C, 45.65; H, 5.94. Found: C, 45.26; H, 5.82.

Our conclusion that the tosyl substituent is introduced into the primary position of $\beta$-cyclodextrin was based on NMR spectra. Conversion of the monotosylate to the corresponding amine (**1**) or amide (**2**) allowed us to

$(CD){-}CH_2NH_2$

1



2

observe protons $\alpha$ to nitrogen satisfactorily separated from other absorptions. Intensities of the $\alpha$-protons (centered at $\delta$ 3.02 and $\delta$ 4.95 for **1** and **2**, respectively) were very close to **2**, strongly supporting the primary substitution.

(9) 6-Deoxy-6-[*N*-(2-aminoethyl)-2-aminoethyl]aminocycloheptaamylose (Ia): Slightly yellow hygroscopic powder (water–acetone); $R_f$ 0.13 (AcOEt/*i*-PrOH/$H_2O$ = 10:13:7), 0.43 (0.2 N aq $NH_3$); NMR (DMSO-$d_6$) $\delta$ 4.83 (7 H, $C_1$ H), 4.3–3.3 (62 H plus trace $H_2O$), 2.8 (10 H, N–$CH_2$); $\delta$ ($D_2O$) 5.1 (7 H, $C_1$ H), 3.8 (40 H), 3.0 (10 H, N–$CH_2$). Ib: NMR ($D_2O$) $\delta$ 5.1 (7 H, $C_1$ H), 3.8 (40 H), 2.9 (14 H, N–$CH_2$).

(10) (a) The stoichiometrical formation of the Ia–$Cu^{2+}$ complex was most clearly demonstrated by a plot of absorbance vs. $Cu^{2+}$ concentration. Thus at a point where $Cu^{2+}$/Ia = 1, a clear inflection was observed, not at the half-saturation point, viz., $Cu^{2+}$/Ia = 0.5. The $Cu^{2+}$ concentration which gives the inflection point was independent of the wavelength observed (550–750 nm).

Furthermore, Cu and Zn complexes of diethylenetriamine are well characterized as a 1:1 complex: N. F. Curtis, *J. Chem. Soc. A*, 1579 (1968); G. R. Cayley and D. N. Hague, *Trans. Faraday Soc.*, **67**, 787 (1971); G. H. McIntyre, Jr., B. P. Block, and W. C. Fernelius, *J. Am. Chem. Soc.*, **81**, 529 (1959). (b) The formation of a 1:2 complex of Cu with cyclodextrin having an ethylenediamine side chain was also reported: Y. Matsui, T. Yokoi, and K. Mochida, *Chem. Lett.*, 1037 (1976); 33rd Annual Meeting of the Chemical Society of Japan in December 1975 (preprint, p 883).

(11) R. L. V. Etten, F. J. Sebastian, G. A. Clowers, and M. L. Bender, *J. Am. Chem. Soc.*, **89**, 3242 (1967).

(12) A control experiment was carried out to estimate how strongly the Zn and Cu complexes of diethylenetriamine bind anions. Addition of zinc diethylenetriamine ($0.3 \times 10^{-2}$–$1.2 \times 10^{-2}$ M) to a sample of naphthalene-1-carboxylate ($9.7 \times 10^{-4}$ M) plus $\beta$-CD ($4.7 \times 10^{-3}$ M) resulted in the decrease in the intensity of the fluorescence which is characteristic to the CD-bound naphthalene-1-carboxylate. By use of the $K_d$ value of $5.47 \times 10^{-3}$ M (pH 10, borate) for the $\beta$-CD–naphthalene-1-carboxylate complex, the $K_d$ value of the ternary complex, zinc (diethylenetriamine)naphthalene-1-carboxylate, was estimated to be $9 \times 10^{-2}$ M; i.e., the binding of carboxylate by the metal complex without the hydrophobic binding site is $1/K_d = 11\ M^{-1}$. A similar conclusion was also drawn for the zinc diethylenetriamine–1,8-ANS complex by the competition technique, giving a smaller $1/K_d$.

Therefore, the observed binding enhancement ($K_d(\beta\text{-CD})/K_d(\text{holohost})$, Table I) is consistent with the assumed anion recognition by the metal ion. Also some stable ternary complexes such as $[Zn(dien)OAc]ClO_4$ are known in a crystalline state, e.g., N. F. Curtis, *J. Chem. Soc. A*, 1579 (1968). This provides us a future possibility that the ternary inclusion complex apohost–metal–anion may be isolated.

Trials to estimate the binding constants of several anions to the copper diethylenetriamine complex were unsuccessful owing to (i) serious disturbance on ANS fluorescence caused by Cu ion and (ii) a lack of an appreciable change in spectroscopic property for quantitative analysis when the Cu complex binds an anion.

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*Received March 1, 1977*

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# Book Reviews

**The Principles of Inorganic Chemistry.** By WILLIAM L. JOLLY (University of California, Berkeley). McGraw-Hill, Inc., New York, N.Y. 1975. vii + 376 pp. $16.00.

This book is virtually a handbook of the *principles* of inorganic chemistry. The chapters are tight and concise and generous use is made of references to more detailed discussions in other inorganic and more specialized texts and to the more readily available journals. A tremendous amount of valuable data is concentrated in numerous tables dispersed throughout the book. In accordance with the author's stated intent, reaction chemistry is essentially limited to examples (mostly from the recent literature) which illustrate the principles under discussion.

The standard topics of "physical-inorganic" chemistry are all covered, including an excellent, short introduction to MO theory (with several tables of Slater AO overlap integrals) and a detailed discussion of the uses of Latimer diagrams in treating aqueous solution chemistry. About one-third of the book is devoted to transition metal complexes. There is a chapter covering reactions of molecular hydrogen (which also includes a very brief introduction to kinetics) and chapters on hydrogen compounds and boron hydrides. Of special note are the chapters on semiconductors, solvated electrons, and metals. The latter contains the only discussion, in an inorganic text of which I am aware, of Brewer's development of the relationship between the crystal structure of a pure metal or alloy and the electron population of the valence orbitals. There are also appendices giving a brief introduction to the terminology of group theory and to the determination of term symbols for free atoms and ions.

The book is meant to be used in the classroom and provides an excellent framework upon which the instructor can (and must) build. It is probably most appropriate for a junior-level inorganic course; a course in physical chemistry is not a prerequisite. The better the background of the students, the more the instructor will want to expand upon the text. Nearly every chapter contains homework problems, many of which cover material not explicitly discussed in the text. The answers to several problems are provided in an appendix.

There are caveats. By equating "ionization potentials" and "electron binding energies", and thereby introducing a discussion of ESCA, the author makes some potentially confusing and misleading statements, expecially for the novice. In discussing the relationships among $\Delta G°$, $\mathcal{E}°$, $\mathcal{E}$, and $K$, the constant 0.05916 is introduced with no indication of its origin and no effective mention of its temperature dependence. Though reference is made to Linnett's book, the discussion of his "double quartet" theory may be too short to be of any value. Thus, an instructor choosing to use this book must read it carefully and find the pitfalls before his/her students do.

For the chemist who has paid little attention to inorganic chemistry during the past decade or so, this short book will provide an overview of the discipline in bite-size pieces. For the practicing inorganic chemist the text may provide a new way of looking at some familiar ideas. I doubt that it is the author's intention that this book serve as a graduate level text and, considering its lack of detailed discussions and its limited descriptive chemistry, it cannot be recommended as such. It can, of course, be used for supplemental readings at the graduate level.

**Mark B. Freilich,** *California State University, Hayward*

**Infrared Absorption Spectroscopy. Second Edition.** By KOJI NAKANISHI (Columbia University) and PHILLIPPA H. SOLOMON (Rutgers University). Holden-Day, Inc., San Francisco, Calif. 1977. x + 287 pp. $10.95.

This is the second edition of a volume that has become a standard for organic chemists since it first appeared in 1962. While most of the data are identical with those given in the first edition, there have been some very welcome additions. A new chapter on Laser Raman Spectroscopy has been incorporated as have sections concerning the characteristic IR bands of substituted pyridines and silicon compounds. Also, the table pertaining to phosphorus-containing compounds has been greatly expanded. References through 1976 have been included as have 15 additional problems (for a total of 100). In addition to a general index, a new index of compounds whose spectra appear in the text has been included. More emphasis is also given to NMR spectroscopy.

The only shortcomings are that this is a soft-covered volume which may not stand up to the use it will need to take, and the thumb-indexing feature of the first edition which was found to be so useful has been deleted.

It is gratifying that this volume has been up-dated. Its low cost will make it accessible to all chemists.

**Howard S. Friedman,** *University of Michigan*