attainment of equilibrium with Meisenheimer complex involves intermediates **2c** and **3c**, which can be observed spectrally. We have also made similar observations for reactions of OH^- with 2,4-dinitrobenzene, 2,4-dinitronaphthalene, quinazoline, 3,5-dinitropyridine, and 5-nitropyridine and -pyrimidine and their halo derivatives.

Scheme I accords with other evidence, e.g., formation of a 3-Meisenheimer complex from OMe^- and **1a** in MeOD.[14] Radical reactions often accompany nucleophilic addition and substitution and anion radicals are known in similar systems.[15] If O_2 is bubbled into an equilibriated solution of **1c** and **5c** in aqueous 0.5 M OH^-, **6** is formed with a similar $1/\tau$ (2.2×10^{-4} s^{-1}) as for the disappearance of the Meisenheimer complex (2.5×10^{-4} s^{-1}), and O_2 should trap **3c**, but not the other species.[16] There is rapid hydrogen exchange at C-2 of 1,3-dinitrobenzene in Me_2SO–D_2O (66:34 v/v, 0.053 M OD^-), but with heating to 50 °C all the proton NMR signals disappear, probably due to line broadening. All reappear on cooling, except at C-2.[17]

Some of the reported rate constants for reaction of OH^- with **1a,b** are in fact for conversion of a 3-Meisenheimer complex (**4a,b**) into picrate ion.[5a,18] To this extent care has to be taken in comparing reactivities of arenes and chloroarenes with OH^-. However, the data in Table I suggest that some steps are faster with **1c** than with **1a,b**, with a complex dependence on solvent composition and [OH^-].

Acknowledgment. Support by the National Science Foundation (Chemical Dynamics Program) and CNR (Rome) is gratefully acknowledged.

(14) Crampton, M. R.; El Ghanani, M. A.; Khan, H. A. *Tetrahedron* **1972**, *28*, 3299.
(15) Russell, G. A.; Janzen, E. G. *J. Am. Chem. Soc.* **1964**, *86*, 1807. Bellobono, T. R.; Gamba, A.; Sala, G.; Tampieri, M. *Ibid.* **1972**, *94*, 5781. Mariani, C.; Modena, G.; Piazzo, G. P.; Scorrano, G. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1187.
(16) Isolated Meisenheimer complexes are not reported to react readily with O_2.[2]
(17) 1,3-Dinitrobenzene does not form a Meisenheimer complex in OD^-–D_2O, but one forms with OH^- in aqueous Me_2SO.
(18) Gibson, B.; Crampton, M. R. *J. Chem. Soc., Perkin Trans. 2* **1979**, 648. Bunton, C. A.; Ihara, Y.; Wright, J. L. *J. Org. Chem.* **1976**, *41*, 2520.

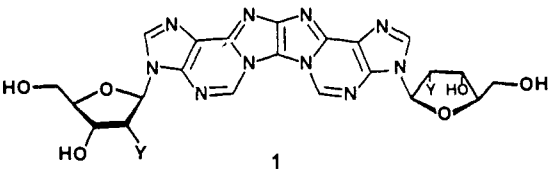
Synthesis of Covalently Linked Double-Helical Cross Sections Representative of Purine–Purine and Pyrimidine–Pyrimidine Duplexes

Nelson J. Leonard* and Balekudru Devadas

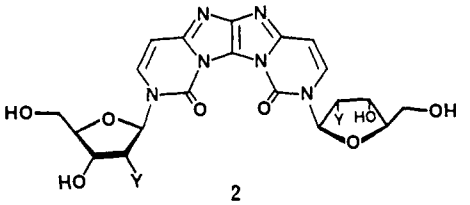
Roger Adams Laboratory, School of Chemical Sciences
University of Illinois, Urbana, Illinois 61801-3731

Received July 11, 1986

We have introduced the concept of covalently linked cross sections with molecular architecture similar to Watson–Crick hydrogen-bonded base pairs in a double helix, and we have shown how these can be synthesized conveniently.[1] The covalent cross sections possess 1,3,4,6-tetraazapentalene as the central linking system, the geometry of which mimics closely that of the doubly hydrogen bonded eight-membered central ring of a normal Watson–Crick cross section. In fact, it would be difficult to construct a closer mimic because of the excellent fit (within 0.2 Å, purine C1′ to pyrimidine C1′) and the coincidence of polarity of the two central ring systems. Great interest in the effect of DNA distortion on binding and biological activity has stimulated us to provide a covalently linked purine–purine cross section **1** with dimensions such as would be produced in the pairing of A with I, capable of generating a bulge in a double-helical RNA or DNA. We also provide a covalently linked pyrimidine–pyrimidine cross section **2** such as might be produced in the hypothetical pairing of C with U or T, namely, a pinched-in RNA or DNA cross section. Fixed-cross-section entities have not been available before this.



1



2

a, Y = OH
b, Y = H

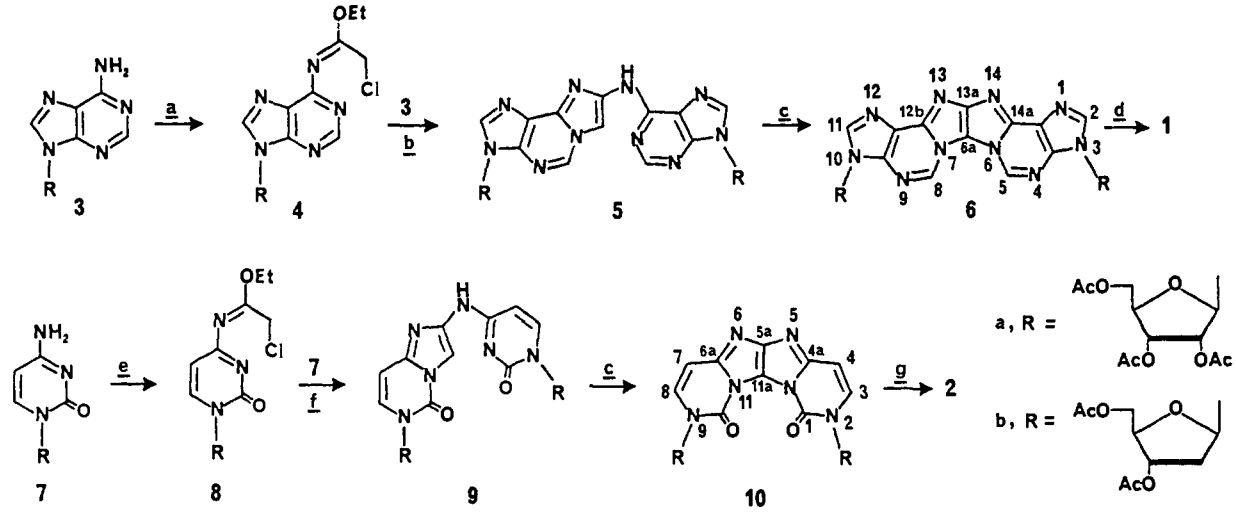
The synthetic Scheme (Scheme I) that culminated in **1a** consisted of three steps from 2′,3′,5′-tri-*O*-acetyladenosine (**3a**) plus final O-deprotection. The intermediate **4a**[2] obtained from **3a** and chloroketene diethyl acetal as described previously[1] was condensed with additional **3a** in the presence of an acid catalyst to give **5a**. The conversion to **5a** was improved to 17% by the use of 0.5 equiv of *p*-toluenesulfonic acid instead of 0.2 equiv.[1] The yield of the highly fluorescent **6a** on oxidative cyclization of **5a** was significantly increased to 40% over that realized with iodobenzene diacetate in trifluoroethanol–nitromethane. This was effected by the use of 2-nitroiodobenzene diacetate in a solvent mixture of 1,1,1,3,3,3-hexafluoro-2-propanol or 1,1,1,3,3,3-hexafluoro-2-methyl-2-propanol and nitromethane. The structures of the intermediates were confirmed by elemental, ^1H NMR, and FAB mass spectral analysis. The symmetry of **6a** was evident from the dramatic simplification of its ^1H NMR spectrum in comparison with that of its immediate precursor **5a**. Particularly diagnostic is the downfield shift[2] of the NMR signal for the proton on the pyrimidine ring observed in the conversion of **3a** to **5a** (0.46 ppm) and again in the conversion of **5a** to **6a** (0.61 ppm). The presence of a plane of symmetry in **6a**, consistent with the assigned structure, was established by its ^{13}C spectrum, in which the chemical shifts of the different junctional carbons 6a and 13a appeared at 111.41 and 152.51 ppm, respectively, and that of the identical junctional carbons 12b and 14a appeared at 141.45 ppm. The structure of **6a** was further established by $^1H/^{13}C$ short-range[3] and long-range[4,5] NMR correlation studies and by high-resolution FAB mass spectrometry.

Complete deacetylation of **6a** was achieved in methanolic ammonia during 1 h at 0 °C followed by 2.5 h at room temperature to give 3,10-di-β-D-ribofuranosylpurino[1″,6″:1′,2′]-imidazo-[4′,5′:4,5]imidazo[2,1-*i*]purine (**1a**) (80%).[6] The 3,10-bis(2′-deoxy-β-D-ribofuranosyl) analogue **1b** (68% yield in deacetylation) was synthesized by a similar sequence starting with 3′,5′-di-*O*-acetyl-2′-deoxyadenosine. Structures of the intermediates and final product **1b** in this sequence were established by the same analytical and spectroscopic means as in the series of reactions leading to **1a**. The precedents[1,7] for the oxidative cyclization step were modified as described above for **1a**.

(1) Devadas, B.; Leonard, N. J. *J. Am. Chem. Soc.* **1986**, *108*, 5012.
(2) Leonard, N. J.; Cruickshank, K. A. *J. Org. Chem.* **1985**, *50*, 2480.
(3) Benn, R.; Gunther, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 350.
(4) Bleick, H.; Gould, S.; Pitner, P.; Wilde, J. *J. Magn. Reson.* **1984**, *56*, 515.
(5) Sato, Y.; Geckle, M.; Gould, S. J. *Tetrahedron Lett.* **1985**, *26*, 4019.
(6) We are grateful to Dr. Kurt L. Loening, Director of Nomenclature, Chemical Abstracts Service for his assistance in providing acceptable IUPAC/CA names for the compounds described herein.
(7) Cruickshank, K. A.; Sumoto, K.; Leonard, N. J. *Tetrahedron Lett.* **1985**, *26*, 2723.

0002-7863/87/1509-0623$01.50/0

Scheme I[a]



[a] (a) Chloroketene diethyl acetal, TsOH, EtOAc, 60 °C, 16 h; (b) TsOH, $C_6H_6/CH_2Cl_2/CH_3CN$ (3:2:1 v/v), 80 °C, 72 h; (c) 2-nitroiodobenzene diacetate, $(CF_3)_2CMeOH/CH_3NO_2$ (1:2 v/v), −10 °C, 1 h; (d) NH_3/MeOH, 0 °C, 1 h, room temperature, 2.5 h; (e) chloroketene diethyl acetal, CH_3CN, room temperature, 21 h; (f) TsOH, C_6H_6/CH_3CN (2:1 v/v), 60 °C, 40 h; (g) NH_3/MeOH, −5 °C, 2 h.

Compounds **1a** and **1b**, which exhibit blue fluorescence and which contain a fused six ring, 10-nitrogen heterocyclic base moiety, correspond in cross section to an A–I base pair that is hydrogen bonded in an extended Watson–Crick manner. There is some ambiguity about the interbase hydrogen bonding in helical poly(A)·poly(I),[8-11] whereas in the three-stranded helical complex poly(A)·poly(I)·poly(I),[8,10-15] one set of base pairs is believed to be of an extended Watson–Crick type, N1 to N1 and N6 to O6, and the other, of the Hoogsteen variety, N7 to N1 and N6 to O6.[16] The extended base pair, by modeling, would have a longer C1′–C1′ distance (13.0 Å) than a standard Watson–Crick base pair (10.67 Å).[11] The base pair I·A within ordered duplexes has been shown to be less stable than I·C[17] and to be strongly affected by the neighboring bases in the sequence.[17]

Compound **2a** mimics a hypothetical C–U base pair in which the carbonyls are constrained to proximity. This is unlike any presently observed structural feature since pyrimidine–pyrimidine bases opposite each other in a natural RNA (U–U in the R17 virus[18,19]) and in a synthetic oligomer (C's between runs of poly(A) and poly(U)[20]) are turned outward.[21] In a thorough study of mismatches by the thermodynamics of double-helix formation, pyrimidine–pyrimidine oppositions such as T·C[22] are strongly destabilizing.[23] Our synthesis of **2a** was initiated with the formation of N^4-(1-ethoxy-2-chloroethylidene)-2′,3′,5′-tri-*O*-acetylcytidine (**8a**)[2] by the action of chloroketene diethyl acetal on 2′,3′,5′-tri-*O*-acetylcytidine (**7a**), followed by reaction with another molecule of **7a** in the presence of *p*-toluenesulfonic acid, oxidative cyclization of **9a** to **10a** (36%), and treatment of **10a** with ammonia to effect O-deprotection. The structures of the intermediates and final product, 2,9-di-β-D-ribofuranosylpyrimido[1″,6″:1′,2′]imidazo[4′,5′:4,5]imidazo[1,2-*c*]pyrimidine-1,10-dione (**2a**),[6] were established by elemental analysis, high-resolution FAB mass spectral data, and ^1H and ^{13}C NMR spectra, including $^1H/^{13}C$ correlation studies. The 2,9-bis(2′-deoxy-β-D-ribofuranosyl) analogue **2b** was synthesized in a similar manner from 3′,5′-di-*O*-acetyl-2-deoxycytidine (**7b**). Both **2a** and **2b** show blue fluorescence.

In conclusion, we have prepared covalently linked purine–purine types **1a** and **1b** that resemble a "long base pair"[11] bulge in a double-helical RNA or DNA cross section. We have also synthesized covalently linked pyrimidine–pyrimidine types **2a** and **2b** that correspond to a hypothetical "short base pair", analogous to a pinched-in RNA or DNA cross section. These offer the advantage over intercalating models[24] of providing a fixed cross section with an established (derived)[25,26] short distance, 8.2 Å, between C1′ and C1′ of the sugar moieties. Compounds **1a,b** and **2a,b**, when phosphorylated and incorporated in a double-helical polynucleotide sequence, will introduce a distortion of known dimensions as a marker for potential alteration in biological activity. The fluorescence properties of these compounds render them suitable probes to be examined by their fluorescent yields, lifetimes, and polarizations.

Acknowledgment. This work was supported by research grant CHE-84-16336 from the National Science Foundation and in part by an unrestricted grant from Eli Lilly and Co. Initial experiments directed at covalently linked DNA/RNA cross sections were performed by Dr. K. A. Cruickshank.

(8) Rich, A. *Nature (London)* **1958**, *181*, 521.
(9) Michelson, A. M.; Monny, C.; Laursen, R. A.; Leonard, N. J. *Biochim. Biophys. Acta* **1966**, *119*, 258.
(10) Michelson, A. M.; Massoulié, J.; Guschlbauer, W. *Prog. Nucl. Acid Res. Mol. Biol.* **1967**, *6*, 83 (see especially p 116).
(11) Saenger, W. *Principles of Nucleic Acid Structure*; Springer-Verlag: New York, 1983; especially pp 120, 129, 157, 246.
(12) Doty, P.; Boedtker, H.; Fresco, J. R.; Haselkorn, R.; Litt, M. *Proc. Natl. Acad. Sci. U.S.A.* **1959**, *45*, 482.
(13) Sigler, P. B.; Davies, D. R.; Miles, H. T. *J. Mol. Biol.* **1962**, *5*, 709.
(14) Arnott, S.; Selsing, E. *J. Mol. Biol.* **1974**, *88*, 509.
(15) Arnott, S.; Bond, P. J.; Selsing, E.; Smith, P. J. C. *Nucl. Acids Res.* **1976**, *3*, 2459.
(16) As in the complex of 9-ethyl-8-bromoadenine and 9-ethyl-8-bromohypoxanthine: Sakore, T. D.; Sobell, H. M. *J. Mol. Biol.* **1969**, *43*, 77.
(17) Martin, F. H.; Castro, M. M.; Aboul-ela, F.; Tinoco, I., Jr. *Nucl. Acids Res.* **1985**, *13*, 8927.
(18) Tinoco, I., Jr.; Borer, P. N.; Dengler, B.; Levine, M. D.; Uhlenbeck, O. C.; Crothers, D. M.; Gralla, J. *Nature (London), New Biol.* **1973**, *246*, 40.
(19) Borer, P. N.; Dengler, B.; Tinoco, I., Jr.; Uhlenbeck, O. C. *J. Mol. Biol.* **1974**, *86*, 843.
(20) Uhlenbeck, O. C.; Martin, F. H.; Doty, P. *J. Mol. Biol.* **1971**, *57*, 217. $(Ap)_nUpC(pU)_n$ was not examined.
(21) Pyrimidine bases are turned outward in single-helical cases: d(pTpT) (Camerman, N.; Fawcett, J. K.; Camerman, A. *J. Mol. Biol.* **1976**, *107*, 601) and poly(C) (Zmudzka, B.; Janion, C.; Shugar, D. *Biochem. Biophys. Res. Commun.* **1969**, *37*, 895. Alderfer, J.; Tazawa, I.; Tazawa, S.; Ts'o, P. O. P. *Biophys. J.* **1975**, *15*, 29a. Broido, M. S.; Kearns, D. R. *J. Am. Chem. Soc.* **1982**, *104*, 5207).
(22) Keepers, J. W.; Schmidt, P.; James, T. L.; Kollman, P. A. *Biopolymers* **1984**, *23*, 2901.
(23) Aboul-ela, F.; Koh, D.; Tinoco, I., Jr.; Martin, F. H. *Nucl. Acids Res.* **1985**, *13*, 4811.
(24) (a) Viswamitra, M. A.; Pandit, J. *J. Biomol. Struct. Dyn.* **1983**, *1*, 743. (b) Viswamitra, M. A.; Pandit, J. *J. Curr. Sci.* **1983**, *52*, 207. (c) Pandit, J.; Seshadri, J. P.; Viswamitra, M. A. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1983**, *C39*, 342.
(25) Wang, A. H.-J.; Barrio, J. R.; Paul, I. C. *J. Am. Chem. Soc.* **1976**, *98*, 7401. The C1′–C1′ distance was calculated from the atomic coordinates for the "half"-molecule, εCyd, by Dr. Scott R. Wilson.
(26) Jakolski, M.; Krzyzosiak, W.; Sierzputowska-Gracz H.; Wiewiorowski, M. *Nucl. Acids Res.* **1981**, *9*, 5423.

Supplementary Material Available: Analytical details, including ^1H and ^{13}C NMR, high-resolution MS, and elemental analyses (4 pages). Ordering information is given on any current masthead page.

*Book Reviews**

Carbohydrate Chemistry. Volume 17. Part I. A Specialist Periodical Report. Senior Reporter: N. R. Williams (University of London). Reporters: B. E. Davison, R. J. Ferrier, and R. H. Furneaux. The Royal Society of Chemistry: London. 1985. XI + 275 pp. $87.00. ISBN 0-85186-182-2.

"The Specialist Periodical Report—Carbohydrate Chemistry" series has been indispensable for more than 15 years to almost anyone interested in the carbohydrates. Part I of the 17th volume of this series retains the camera-ready format that was introduced in Volume 15 and describes the chemistry of mono-, di-, and trisaccharides and their derivatives.

There are 24 chapters: Introduction; Free Sugars, Glycosides and Disaccharides; Oligosaccharides; Ethers and Anhydro-sugars; Acetals; Esters; Halogeno-sugars; Amino-sugars; Miscellaneous nitrogen Derivatives; Thio-sugars; Deoxy-sugars; Unsaturated Derivatives; Branched-chain Sugars; Alduloses, Dialdoses, and Diuloses; Sugar Acids and Lactones; Inorganic Derivatives; Alditols and Cyclitols; Antibiotics, Nucleosides; NMR Spectroscopy and Conformational Features; Other Physical Methods; Separatory and Analytical Methods; Synthesis of Enantiomerically Pure Non-carbohydrate Compounds. Each chapter contains a summary of important developments in this field, including a citation of recent review articles at the beginning. The references appear to cover the literature published through 1983 (available by February 1984) and are conveniently placed at the end of each chapter. Over 1400 references are listed (compared to 1200 in Volume 16), and the variety of journals represented indicates the growing international scope of this fascinating chemistry. To accommodate the increasing trend in oligosaccharides, the authors have introduced a separate chapter on oligosaccharides, to include trisaccharides, tetrasaccharides, and higher saccharides.

The chapter contains 60 references which clearly demonstrates actual interest.

In view of increasing importance of carbohydrate synthons in organic synthesis, the last chapter Synthesis of Enantiomerically Pure Non-Carbohydrate Compounds, that was introduced in Volume 9 and modified in Volume 14, is highly valuable and contains 57 references (compared to 38 in Volume 16). Also the chapters on deoxy, branched, free, and amino sugars cover recent advances in syntheses from non-carbohydrate precursors, a field of increasing interest in recent years. An improved author index is also provided with references to each chapter, and it adds greatly to the usefulness of the volume. This series has, over the years, been characterized by a standard of editorial excellence. The present volume is no exception, and any errors of editing or typing are insignificant.

This volume, together with its predecessors, should be in every chemical library, and it is an indispensable item in the personal library of anyone working in the carbohydrate field.

Zbigniew J. Witczak, *Purdue University*

Volumes of Proceedings

Large-Scale Mammalian Cell Culture. Edited by Joseph Feder and William R. Tolbert (Monsanto Co.). Academic Press: Orlando, FL. 1985. x + 159 pp. $25.00. ISBN 0-12-250430-5.

A collection of nine papers and two panel discussions from an ACS symposium held in Philadelphia in 1984. Biochemical aspects are prominent.

Evaluation of Pesticides in Ground Water. Edited by Willa Y. Garner, Richard C. Honeycutt, and Herbert N. Nigg. American Chemical Society: Washington, DC. 1986. x + 573 pp. $94.95. ISBN 0-8412-0979-0.

There are 32 typescript papers in this volume, grouped under the headings Physical and Chemical Parameters, Ground Water Monitoring Techniques, Modeling and Model Valuation, Risk Assessment and its Toxicological Significance, and Regulatory Aspects. The 16-page index is exemplary.

Strong Metal–Support Interactions. Edited by R. T. K. Baker, S. J. Tauster, and J. A. Dumesic. American Chemical Society: Washington, DC. 1986. x + 238 pp. $44.95. ISBN 0-8412-0955-3.

The nature and action of metal catalysts on solid supports, especially from the standpoint of industrial processes, were the subjects of a symposium held in Miami Beach in 1985. The typescripts of 21 papers, together with an 8-page index, make up this volume.

Xenobiotic Conjugation Chemistry. Edited by Gaylord D. Paulson, John Caldwell, David H. Hutson, and Julius J. Menn. American Chemical Society: Washington, DC. 1986. x + 358 pp. $49.95. ISBN 0-8412-0957-X.

The fate of foreign chemical substances to which the living body is exposed is an increasingly important subject. The compounds into which they are converted may lead to a detoxification process, but in some cases they may themselves have even greater activity than the original substance. The 1985 symposium on which this book is based produced 16 papers dealing with isolation, identification, and biological significance of these xenobiotic conjugates. Thoroughly indexed.

Biological Methylation and Drug Design: Experimental and Clinical Role of *S*-Adenosylmethionine. Edited by Ronald T. Borchardt, Cyrus R. Creveling, and Per Magne Ueland. Humana Press: Clifton, NJ. 1986. xxii + 457 pp. $69.50. ISBN 0-89603-102-0.

The proceedings of a symposium on the Biochemistry of *S*-Adenosylmethionine as a Basis for Drug Design, held in Norway in 1985, have been elaborated into a series of chapters by the plenary speakers. They are arranged in the areas Protein and Phospholipid Methylations, Nucleic Acid Methylations, Regulation of *S*-Adenosylmethionine, *S*-Adenosylhomocysteine and Methylthioadenosine Metabolism, Clinical Aspects, and Design, Synthesis and Biological Evaluation of Transmethylation Inhibitors. Indexed.

Dynamical Processes and Ordering on Solid Surfaces. Edited by A. Yoshimori and M. Tsukada. Springer-Verlag: Berlin and New York. 1985. xii + 195 pp. $24.00. ISBN 0-387-15108-7.

The Seventh Taniguchi Symposium, held in Japan in 1984, was concerned with the physical chemistry of collisions, optical processes at surfaces, and ordering of adsolved materials. The typescripts of the papers appear in this volume, which has no subject index.

Polycrystalline Semiconductors: Physical Properties and Applications. Edited by G. Harbeke. Springer-Verlag: Berlin and New York. 1985. viii + 245 pp. $29.50. ISBN 0-387-15143-5.

A symposium on materials science and technology, held in Italy in 1984, was the source of the typescript papers in this volume. There is much concern with the nature of grain boundaries and with polycrystalline silicon. Not indexed.

Ion Formation from Organic Solids. Edited by A. Benninghaven. Springer-Verlag: Heidelberg and New York. 1986. 219 pp. $34.00. ISBN 3-540-16258-5.

Proceedings of the 3rd International Conference on the title subject, held at the University of Münster in 1985, consisting of 40 papers in such areas as ^{252}Cf-plasma desorption, SIMS, other methods of formulation of organic ions, instrumentation, FT ion cyclotron resonance. Set in tyype, but not indexed.

Modern Chlor-Alkali Technology. Volume 3. Edited by K. Wa'l. Ellis Horwood: Chichester; John Wiley & Sons: New York. 1986. 450 pp. $140.00. ISBN 0470-20317-X.

Thirty papers, from the areas of business outlook, safety, development and operation of membrane cells, electrodes, plant design, and hypochlorite and chlorate production, make up this typeset volume, which deserves an index longer than the two pages allotted to it.

Flavonoids and Bioflavonoids, 1985. Edited by L. Farkas, M. Gâbor, and F. Kâllay. Elsevier Science Publishers: Amsterdam and New York.

*Unsigned book reviews are by the Book Review Editor.