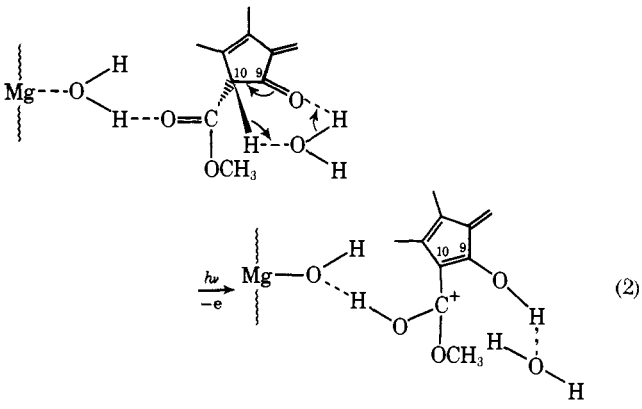

(2)

β-keto ester function may possibly be duplicated by an amide or hydroxyl group of the reaction center lipoprotein complex.

We have thus fully specified the role of the ring V β-keto ester group in the photosystem I primary light reaction. The expected[4a] conformation change in B during reaction 2 may provide the mechanism for the energization of the photosynthetic membrane.[17] Experiments are underway to confirm the above interpretations by an NMR spectroscopic determination of the proposed photoenolization process under conditions comparable to those of the present study. We are aware of the fact that our present conclusions appear to be generally consistent with the recognized role of the cyclopentanone ring in the epimerization of Chl a to Chl a′ involving the C-10 hydrogen in protic solvents.[18] We have also begun a parallel series of studies on pyrochlorophyll photoactivity in order to delineate water enhancement effects other than the photoenolization interpretation given above. In pyroChl the C10 carbomethoxy group in Chl a has been replaced by a hydrogen atom, and no photoenolization in ring V is possible.

Acknowledgment. The work reported in this communication was supported by the Alcoa Foundation and the National Science Foundation.

References and Notes

(1) This work was presented by F. K. Fong as part of the Michael Faraday Lecture delivered in the 9th Midwest Theoretical Chemistry Conference held at the Northern Illinois University, DeKalb, Ill., May 21, 1976.
(2) F. K. Fong and V. J. Koester, *Biochim. Biophys. Acta*, **423**, 52 (1976).
(3) (a) F. K. Fong, V. J. Koester, and J. S. Polles, *J. Am. Chem. Soc.*, **98**, 6406 (1976); (b) V. J. Koester and F. K. Fong, *J. Phys. Chem.*, **80**, 2310 (1976).
(4) For a review of recent development, see (a) F. K. Fong, "Theory of Molecular Relaxation: Applications in Chemistry and Biology", Wiley-Interscience, New York, N.Y., 1975, Chapter 9; (b) translated into Japanese by Y. Inoue, *Protein, Nucleic Acid Enzyme*, **21** (9), 701 (1976); (c) *Acc. Chem. Res.* **9**, 433 (1976); (d) "The Primary Light Reaction in Photosynthesis: A Molecular Interpretation", Wiley-Interscience, New York, N.Y., in press.
(5) For related discussions, see R. S. Knox in "Topics in Photosynthesis", Vol. II, J. Barber, Ed., Elsevier, New York, N.Y., in press.
(6) T. S. Rahman and R. S. Knox, *Phys. Status Solidi*, **58**, 715 (1973).
(7) F. K. Fong, *J. Am. Chem. Soc.*, submitted for publication.
(8) V. B. Evstigneev and A. N. Terenin, *Dokl. Akad. Nauk SSSR*, **81**, 223 (1951).
(9) F. K. Fong and N. Winograd, *J. Am. Chem. Soc.*, **98**, 2287 (1976).
(10) (a) E. K. Putseiko in "Elementary Photoprocesses in Molecules", Bertol'd S. Neporent, Ed., Consultants Bureau, New York, N.Y., 1968, p 281; (b) A. N. Terenin, E. Putseiko, and I. Akimor, *Discuss. Faraday Soc.*, **27**, 83 (1959).
(11) (a) C. W. Tang and A. C. Albrecht, *J. Chem. Phys.*, **62**, 2139 (1975); **63**, 953 (1975); (b) C. W. Tang, F. Douglas, and A. C. Albrecht, *J. Phys. Chem.*, **79**, 2823 (1975); (c) C. W. Tang and C. A. Albrecht, *Mol. Cryst. Liq. Cryst.*, **25**, 53 (1974).
(12) (a) F. K. Fong and V. J. Koester, *J. Am. Chem. Soc.*, **97**, 6888 (1975); (b) F. K. Fong, *ibid.*, **97**, 6890 (1975).
(13) A. S. Holt and E. E. Jacobs, *Am. J. Bot.*, **41**, 710 (1954).
(14) N. Winograd, A. Shepard, D. H. Karweik, V. J. Koester, and F. K. Fong, *J. Am. Chem. Soc.*, **98**, 2369 (1976).
(15) See, for example, R. E. Fenna and B. W. Mathews, *Nature (London)*, **258**, 573 (1975). These authors have established that a basic unit of bacterial antenna system in chlorobium *limicola* is a cluster monomeric Chl a–protein complexes.
(16) Reference 4a, p 258.
(17) F. K. Fong, *J. Am. Chem. Soc.*, **98**, 7840 (1976).
(18) H. H. Strain, *J. Agr. Food Chem.*, **2**, 1222 (1954).
(19) Alfred P. Sloan Foundation Fellowship, 1974–1978.

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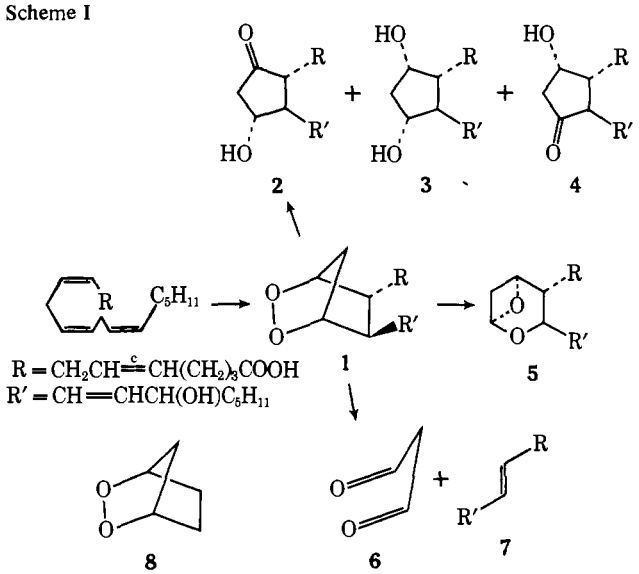
Synthesis and Thermal Reactivity of Some 2,3-Dioxabicyclo[2.2.1]heptane Models of Prostaglandin Endoperoxides

Sir:

Prostaglandin (PG) endoperoxides[1] (e.g., **1**), the immediate biological precursors of prostaglandins (e.g., **2, 3, 4**) and thromboxanes[2] (e.g., **5**), are generally considered to be derivatives of the otherwise unknown 2,3-dioxabicyclo[2.2.1]heptane (**8**) heterobicyclic ring system. Recently, solutions containing PG endoperoxides, PGG_2 and PGH_2, were prepared enzymatically.[3] However, studies of the chemical reactions of these key biomolecules are beclouded by the instability[4] and uncertain purity[5] of samples obtained by bioconversion. We now report: (1) the first nonenzymatic synthesis of bona fide, fully characterized derivatives of the bicyclic ring system **8**, (2) thermal fragmentation of **10**, a derivative of **8**, to a 1,3-dione and olefin, which is reminiscent of the in vitro fragmentation of PG endoperoxides, and (3) thermochemical data for decomposition of this model endoperoxide which show unexpectedly great thermal stability consistent with a homolytic mechanism rather than a concerted electrocyclic fragmentation.

Scheme I



The unsaturated analogue of **8**, 2,3-dioxabicyclo[2.2.1]-heptene, and substituted derivatives thereof are readily available, though thermally labile.[6] Thus, the unsaturated peroxide **9** is readily prepared by cycloaddition of singlet oxygen[7] with 1,4-diphenyl-1,3-cyclopentadiene (Scheme II).[8] We now find that diimide[9] selectively reduces the C-C π-bond of **9** to give 1,4-diphenyl-2,3-dioxabicyclo[2.2.1]heptane (**10**).[10] The upfield portion of the ^1H NMR spectrum of **10** (Figure 1) in perdeuteriobenzene solution exhibits four multiplets centered at δ 1.90, 2.17, 2.40, and 2.64 which correspond to H_x, H_a, H_n, and H_s, respectively. Geminal coupling J_{xn} = 8 Hz, J_{as} = 10 Hz, and long range W-plan[11] coupling J_{ns} = 2.5 Hz support these assignments. Reduction of **9** with dideuteriodiimide occurs stereospecifically cis-exo to give **11** (Scheme

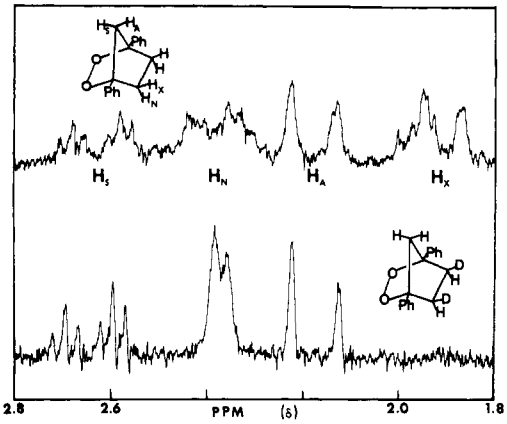
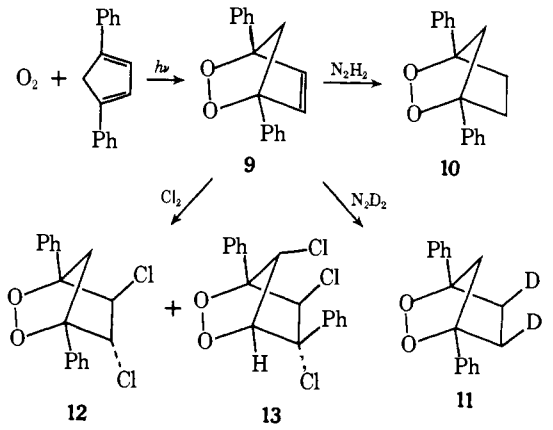


Figure 1. Upfield region of 100-MHz ^{1}H NMR spectra of **10** (top) and **11** (bottom).

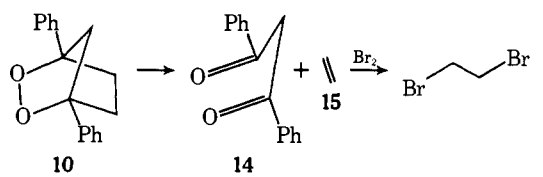
Scheme II



II). The multiplet at δ 1.90 and 8 Hz coupling of H_n with H_x are absent in the ^{1}H NMR spectrum of **11** (Figure 1). The mass spectrum of **11** (*m/e* (relative intensity) 254 (9), 224 (23), 222 (39), 221 (100), 105 (99), 77 (71), 30 (2)) shows fragmentation into $C_2D_2H_2$ and 1,3-diphenyl-1,3-propanedione. In the mass spectrum of **10** there is no fragment of *m/e* 30 and the parent peak appears at 252.

Two products from the chlorination of **9** in CCl_4 were isolated by chromatography on silica gel. The ^{1}H NMR spectra of these compounds support the structures **12**[10] and **13**[10] (Scheme II): 60-MHz ^{1}H NMR (C_6D_6) for peroxide (**12**) δ 7.12 (10 H), 4.66 (t, 1 H, J = 2.8 Hz), 4.55 (d, 1 H, J = 2.8 Hz), 2.96 (d, 1 H, J = 11 Hz), 2.58 (dd, 1 H, J = 2.8, 11 Hz); and for peroxide (**13**) δ 7.13 (10 H), 5.42 (d, 1 H, J = 4.3 Hz), 4.88 (dd, 1 H, J = 2.4, 4.3 Hz), 4.56 (d, 1 H, J = 2.4 Hz).

Decomposition of purified PG-endoperoxides is a complex process involving disproportionation, reduction, and fragmentation.[1i,5] The bridgehead substitution in **10** prohibits PG-endoperoxide-like reactivity involving abstraction of a bridgehead proton such as disproportionation to **2** or **4** (Scheme I). This simplifies examination of reactions involving reorganization of C-O and C-C σ-bonds such as rearrangement to **5** or fragmentation to **6** and **7**. Fragmentation of PG-endoperoxides can be the major reaction pathway accompanying bioconversion of eicosapolyenoic acids in the absence of glutathione,[12] or accompanying thrombin-induced aggregation of human platelets.[13] A fragmentation of the model endoperoxide **10** was observed upon heating a solution in C_6D_6 in

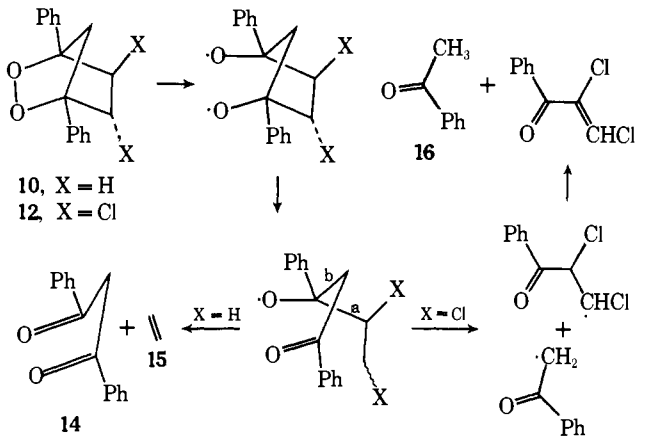


a sealed NMR tube. The ^{1}H NMR spectrum of the reaction product mixture from **10** exhibits sharp singlets at δ 6.56 and 5.27 corresponding to 1,3-diphenyl-1,3-propanedione (**14**) and ethylene (**15**), respectively, in approximately 10% yield each. The presence of ethylene was confirmed by addition of bromine to the thermolysis product mixture and mass spectral identification after gas-liquid phase chromatographic isolation of the 1,2-dibromoethane produced. In contrast, **12**, gives neither **14**, nor dichloroethylene. Rather, acetophenone (**16**) is produced in 26% yield by the thermolysis of **12**. Acetophenone was characterized by ^{1}H NMR and gas-liquid phase chromatographic comparison with an authentic sample.

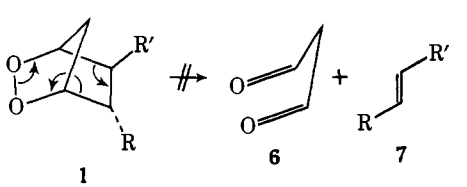
Table I. First-Order Rate Constants for Decomposition of **10**

Temp (°C)	10^5k (s^{-1})	Temp (°C)	10^5k (s^{-1})
120.0	1.39	135.0	7.87
130.8	5.55	140.0	14.99

Scheme III



A preliminary study of the thermolysis kinetics for **10** was made by monitoring the integrated area of the ^{1}H NMR absorptions of the reaction products in the region δ 8.0-7.5. First-order kinetics are followed. The rate constants listed in Table I give E_a = 39 kcal/mol. The same Arrhenius activation energy was reported for thermal decomposition of di-*tert*-butyl peroxide.[14] Thus, a rate determining, homolytic splitting of the O-O bond in **10** is indicated for the thermolysis. Two subsequent β-fissions give **14** and **15**.[12] Production of acetophenone from **12** can also be understood in terms of an initial homolysis of the O-O bond followed by two β-fissions. However, the second β-fission involves bond b rather than bond a (Scheme III).[15] An alternative mechanism involving a concerted reorganization of three bonds is apparently not operative. This is noteworthy since such a process could take advantage of a $[2\sigma_s + 2\sigma_s + 2\sigma_s]$ orbital symmetry allowed pathway,[16] and a high overall exothermicity. These observations suggest that the in vitro fragmentation of PG-endoperoxides, which is often pictured as a concerted bond shift process,[17] is not a simple unimolecular rearrangement. The



activation energy for a stepwise homolytic decomposition of PG-endoperoxides should not differ very greatly from that observed for **10**, and should, thus, be inaccessible under physiological conditions. Therefore, the reaction is probably a catalyzed process.[5] Inhibition of the fragmentation of **1** by glutathione[12] may well involve deactivation of the catalyst.

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References and Notes

(1) (a) P. F. Beal, G. S. Fonken, and J. E. Pike, Belgium Patent 659 984 (1964); (b) B. Samuelsson, *J. Am. Chem. Soc.*, **87**, 3011 (1965); (c) M. Hamberg and B. Samuelsson, *ibid.*, **88**, 2349 (1966); (d) M. Hamberg and B. Samuelsson, *J. Biol. Chem.*, **242**, 5329, 5336, 5344 (1967); (e) B. Samuelsson, *Prog. Biochem. Pharmacol.*, **3**, 59 (1967); (f) B. Samuelsson, *ibid.*, **5**, 109 (1969); (g) B. Samuelsson, *Fed. Proc.*, **31**, 1442 (1972); (h) M. Hamberg and B. Samuelsson, *Proc. Natl. Acad. Sci. U.S.A.*, **70**, 899 (1973); (i) D. H. Nugteren and E. Hazelhof, *Biochim. Biophys. Acta*, **326**, 448 (1973); (j) C. Pace-Asciak and M. Nashat, *ibid.*, **388**, 243 (1975).

(2) (a) M. Hamberg, J. Svensson, and B. Samuelsson, *Proc. Natl. Acad. Sci. U.S.A.*, **72**, 2994 (1975); (b) G. B. Kolata, *Science*, **190**, 770 (1975).

(3) The presence of endoperoxides in these solutions has been inferred by convincing indirect evidence, and recently a solvent-free product was obtained but structural or elemental analytical evidence for their structures remains to be obtained; see ref 1h–j.

(4) For example, 9α,11α-epidioxy-15(*S*)-hydroxy-13-*trans*-prostenoic acid has a half-life of 2.7 h at 20 °C in light petroleum–ether (1:1/v:v) and in aqueous medium the half-life is only 30 min at 20 °C: ref 1i.

(5) Evidence which suggests that these preparations may contain impurities which catalyze their decomposition was obtained recently: W. A. Pryor and J. P. Stanley, *J. Org. Chem.*, **40**, 3615 (1975).

(6) (a) G. O. Schenk and D. E. Dunlap, *Angew. Chem.*, **68**, 248 (1956); (b) K. H. Schutte-Elte, B. Willhalm, and G. Ohloff, *ibid.*, **81**, 1045 (1954); (c) W. R. Adams and D. J. Trecker, *Tetrahedron*, **27**, 2631 (1971); (d) G. O. Schenk, W. Muller, and H. Pfennig, *Naturwissenschaften*, **41**, 374 (1954).

(7) Photolyses were performed in benzene solution in a Pyrex vessel with internal water cooled cold finger and external irradiation with a Rayonette Photochemical Reactor (Southern New England Ultraviolet) using 350-nm lamps: cf. W. Müller, Thesis, Gottingen, 1956, pp 25–26.

(8) N. L. Drake and J. R. Adams, Jr., *J. Am. Chem. Soc.*, **61**, 1326 (1939).

(9) Generated in situ in methanol solution by addition of acetic acid to a suspension of potassium azodicarboxylate.

(10) The peroxides **10**, **11**, **12**, and **13** all gave positive peroxide tests with ferrous thiocyanate reagent: cf. R. A. Johnson and E. G. Nidy, *J. Org. Chem.*, **40**, 1681 (1975). Correct elemental analyses were obtained for these compounds which are all white crystalline solids (from ethanol): **10** mp 109.7–110.0 °C (71% yield); **12** mp 140.5–141.0 °C (26% yield); **13** mp 141.7–142.3 °C (11% yield).

(11) L. M. Jackman and S. Sternhell, "Applications of NMR Spectroscopy in Organic Chemistry", 2nd ed, Pergamon, New York, N.Y., 1959; S. Sternhell, *Q. Rev., Chem. Soc.*, **23**, 236 (1969).

(12) D. H. Nugteren, R. K. Beerthuis, and D. A. Van Drop, *Recl. Trav. Chim. Pays-Bas*, **85**, 405 (1966).

(13) M. Hamberg, J. Svensson, and B. Samuelsson, *Proc. Natl. Acad. Sci. U.S.A.*, **71**, 3824 (1974); PG-endoperoxides are metabolized almost exclusively to nonprostanoic acid derivatives in this process.

(14) (a) J. H. Raley, F. F. Rust, and W. E. Vaughan, *J. Am. Chem. Soc.*, **70**, 1336 (1948); (b) C. F. H. Tipper, *J. Chem. Soc.*, 1675 (1953); (c) A. R. Blake and K. O. Kutschke, *Can. J. Chem.*, **37**, 1462 (1959).

(15) The vicinal chloro substituent might discourage fission of bond a by stabilizing the neighboring radical; cf. W. C. Danen and R. L. Winter, *J. Am. Chem. Soc.*, **93**, 716 (1971), and references cited therein.

(16) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).

(17) See, for example, ref 1c.

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Book Reviews

The World of Quantum Chemistry. Edited by R. DAUDEL (Centre de Mécanique Ondulatoire Appliquée) and B. PULLMAN (Institut de Biologie Physico-Chimique). R. Reidel Publishing Co., Dordrecht/Boston. 1974. xiv + 316 pp. $37.00.

The proceedings of the First International Congress of Quantum Chemistry held at Menton, France, in 1973 are reported. Five symposia, chaired by P.-O. Löwdin, J. Koutecký, R. Daudel, R. Parr, and A. Pullman, deal with methods of quantum chemistry, the electronic structure and conformations of molecules, theory of chemical reactivity, the formation and evolution of molecular excited states, and environmental effects on molecules. These symposia are not intended to provide a comprehensive treatise of each subject; rather, they should be viewed as a perspective provided by several distinguished scientists and experts. Contributions range from a reporting of calculated results to an exposé of powerful theoretical methods and interpretive remarks. One is introduced to methods and learns of their successful application; however, the lectures are not generally a source for details and alternative approaches are often not discussed.

Professor J. C. Slater sets a discussion of the Xα method in an interesting and informative historical perspective. The excitement about the unfolding applicability of quantum mechanics during the past 50 years is conveyed by one who held much of it in his own hands. E. Davidson discusses the configuration interaction description of electron correlation and some of his own very significant work on the use of natural orbitals in the development and analysis of CI expansions. Some recent developments and current problems of the theory of intermolecular interactions are presented by W. Kolos who discusses perturbation theory, CI and SCF applications.

The second symposium is introduced by Professor J. Koutecky who remarks on simple theories for the calculation of electronic structure. J. Pople reports on the application of the ab initio SCF method using modest basis sets to the problem of internal rotation about single bonds. Results are reported for several molecules, and some discussion of an adequate level of treatment, the effect of polar substituents, and coupled interactions is included. B. Pullman lectures on recent conformational studies using the PCILO method (localized orbitals and local excitations to antibonding orbitals applied at the CNDO level). Implications of preferred conformational space calculations on proteins are discussed with reference to X-ray data, and applications to torsion angles in polynucleotides and conformations of acetylcholine are described.

Professor R. Daudel introduces the third symposium on the theory of chemical reactivity and discusses the use of static and dynamical indexes of reactivity. M. Karplus considers the importance of quantum corrections to classical trajectory calculations of reaction attributes using the hydrogen exchange reaction to illustrate different levels of approximation. Charge and spin transfers in chemical reactions are discussed by K. Fukui with emphasis on orbital interactions. Illustrative reactions are interpreted using highest occupied and lowest unoccupied molecular orbital concepts.

The fourth symposium deals with the formation and evolution of molecular excited states. J. Jortner and S. Mukamel provide a unified theoretical scheme for the description of the diverse decay channels of excited electronic states of polyatomic molecules. This symposium is a much more toward a self-contained development of the subject. The basic principles of relaxation phenomena are presented in terms of a Green's function formalism for the determination of decay amplitudes of the system; interstate coupling schemes and the time evolution of excited molecular states are carefully discussed. E. Heilbronner begins his lecture on UV photoelectron spectroscopy by pointing out possible misunderstandings in the interpretation of data in terms of the theoretical construct of molecular orbitals and Koopmans' theorem. Limitations of the theory, correlations of data with theoretical calculations, and correlations involving closely related compounds are discussed.

The last symposium on environmental effects on molecules is introduced by A. Pullman who considers nonpolar and polar solvents and crystal environmental effects on hydrogen-bonded systems like valinomycin; a supermolecule approach utilizing possibly simple models for nearest neighbor molecules is advocated. A. D. Buckingham lectures on intermolecular forces and the electric and magnetic properties of molecules, concisely setting forth the fundamentals of polarizability and dipole moment effects with brief reference to magnetic susceptibility and nuclear magnetic shielding. O. Sinanoğlu expounds on three types of potentials needed to predict conformations of molecules in solution. The adiabatic potential for molecules in