9-[(*E*)-4-Hydroxy-2-buten-1-yl]guanine (4b). This material was prepared from **34** as described for **4a** and **3c**. UV and NMR spectral data were in accord with literature values.[20,21]

9-(4-Hydroxy-2-butyn-1-yl]guanine (36). Hydrolysis of **35** by the method used for **3c**, followed by recrystallization from H_2O, gave a 68% yield of white solid: mp >235 °C dec (gradual); UV λ_{max} (0.1 M phosphate buffer, pH 7) 252 nm (ϵ 7160); NMR spectrum was in accord with reported values.[19]

9-[(*Z*)-4-(Benzoyloxy)-2-buten-1-yl]adenine (37). By a modification of the procedure used for **26** (reaction temperature 20 °C, preparative TLC plates developed in 90:10:1 $CHCl_3$–MeOH–H_2O, R_f 0.6), **37** was obtained from **29** in 50% yield as a cream-colored solid: mp 154–156 °C; UV λ_{max} (MeOH) 262 nm (ϵ 15 430); 200-MHz NMR ($CDCl_3$) δ 5.06, 5.10 (overlapping d, J = 5.5 Hz, each 2 H, CH_2N, CH_2O), 5.66 (br s, 2 H, NH_2), 5.85–6.1 (m, 2 H, =CH), 7.45–7.65 (m, 3 H, *m,p*-Ph H), 7.95, 8.42 (s, each 1 H, C^2-H, C^8-H), 8.10 (d, J = 7 Hz, 2 H, *o*-Ph H). Anal. ($C_{16}H_{15}N_5O_2$) C, H, N.

9-[(*Z*)-4-Hydroxy-2-buten-1-yl]adenine (38). Treatment of **37** with NaOMe as described for **17b** gave a 50% yield of white solid (recrystallized from MeOH): mp 196–199 °C; TLC in 90:10:1 $CHCl_3$–MeOH–H_2O (R_f 0.3); UV λ_{max} (0.1 M phosphate buffer, pH 7) 261 nm (ϵ 12 000); 200-MHz NMR (Me_2SO-d_6) δ 4.22 (d, J = 5.5 Hz, 2 H, CH_2O), 4.85 (d, J = 6.5 Hz, 2 H, CH_2N), 4.94 (br s, 1 H, OH), 5.55–5.8 (m, 2 H, =CH), 7.24 (br s, 2 H, NH_2), 8.14, 8.17 (s, each 1 H, C^2-H, C^8-H). Anal. ($C_9H_{11}N_5O{\cdot}0.1H_2O$) C, H, N.

Enzyme Assays. Full details of the "staggered" assay conditions have been reported.[51] Briefly, step I (thymidine kinase assay) entailed incubation of the test compound with HSV-1 thymidine kinase for 4 h at 37 °C followed by examination of an aliquot by HPLC for presence of the monophosphate. In step II (phosphorylation to di- and triphosphate), the remainder of the step I assay mixture was treated with extract of HSV-1-infected HeLa cells and hog brain GMP kinase. After incubation overnight at 30 °C, the amounts of mono-, di-, and triphosphate were determined by HPLC. Finally, the mixture from step II was incubated at 37 °C with activated salmon sperm DNA, deoxyribonucleotides including [^{3}H]dTTP, additional crude extract of HSV-1-infected cells, and other factors. The assay was conducted in the presence of $(NH_4)_2SO_4$ to determine viral polymerase activity and in the absence of $(NH_4)_2SO_4$ when the cellular polymerases were assayed. The extent of DNA synthesis was determined by measuring the radioactivity incorporated into washed nucleic acids precipitated by trichloroacetic acid.

In Vitro Antiviral Assays. As previously described,[3,51,52] quadruplicate confluent monolayers of primary rabbit kidney cell cultures, preincubated with serial dilutions of test compound in maintenance medium, were challenged with approximately 10 $TCID_{50}$ of either HSV-1, strain Schooler, or HSV-2, strain Curtis. Cultures were incubated at 37 °C and evaluated for virus-induced cytopathology on day 5. The ED_{50} was calculated as the concentration of drug required to completely suppress development of cytopathology in 50% of the cell monolayers.

Acknowledgment. We thank Corrille M. DeWitt for the in vivo testing of **3a**, Dr. Byron Arison for NMR spectral analyses of **5a,b**, Valorie Mayo for UV spectra, Jack Smith for mass spectra, and the laboratory of Jane Wu for elemental analyses. We are grateful to Alexander Matzuk and Glenn F. Reynolds for scale-ups of key intermediates.

Registry No. **3a**, 116663-96-8; **3b**, 116663-97-9; **3c**, 116664-10-9; **4a**, 99776-29-1; **4b**, 104715-61-9; **5a**, 116663-91-3; **5b**, 116663-90-2; **6a**, 116663-92-4; **6b**, 45467-35-4; **7a**, 116663-93-5; **8a**, 116663-94-6; **8b**, 116663-95-7; **10**, 116663-98-0; **11**, 116698-29-4; **12a**, 710-43-0; **12b**, 115109-28-9; **13a**, 2345-68-8; **13b**, 82442-59-9; **14a**, 116663-99-1; **14b**, 116664-00-7; **15a**, 116664-01-8; **15b**, 116664-02-9; **16a**, 116669-26-2; **16b**, 116669-27-3; **17a**, 116669-28-4; **17b**, 116669-29-5; **18**, 116664-03-0; **19**, 116664-04-1; **20**, 79930-08-8; **21**, 116664-05-2; **22**, 116664-06-3; **23**, 116664-07-4; **24**, 116664-08-5; **25**, 116664-09-6; **26**, 116664-11-0; **27**, 116664-12-1; **28**, 81121-63-3; **29**, 116664-13-2; **30**, 104311-79-7; **32**, 114978-77-7; **33**, 116664-14-3; **34**, 116664-15-4; **35**, 116664-16-5; **36**, 99776-30-4; **37**, 116664-17-6; **38**, 114978-80-2; H_2C=CHCN, 107-13-1; $N_2CHCOOEt$, 623-73-4; $ClCH_2CHO$, 107-20-0; H_2C=COOEt, 140-88-5; $ClCH_2COOEt$, 105-39-5; (*Z*)-$HOCH_2CH$=$CHCH_2OH$, 6117-80-2; (*E*)-$BrCH_2CH$=$CHCH_2Br$, 821-06-7; $HOCH_2C{\equiv}CCH_2OH$, 110-65-6; 6-chloroisocytosine, 1194-21-4; (*Z*)-1,2-cyclopropanedicarboxylic acid, 696-74-2; adenine, 73-24-5; thymine, 65-71-4; 2-amino-6-chloropurine, 10310-21-1.

Additions and Corrections

1987, Volume 30

Rosa L. Lopez de Compadre, R. A. Pearlstein, A. J. Hopfinger,* and J. K. Seydel: A Quantitative Structure–Activity Relationship Analysis of Some 4-Aminodiphenyl Sulfone Antibacterial Agents Using Linear Free Energy and Molecular Modeling Methods.

Page 904. The QSAR given by eq 3 is not valid because the intramolecular entropy, S, was incorrectly computed. The revised QSAR, which replaces eq 3, is

$$pC = 0.040\ (\pm 0.005)P_A + 0.469\ (\pm 0.052)\phi + 5.18\ (\pm 0.06)$$

$$N = 34,\ R = 0.90,\ SD = 0.20,\ F = 63.0$$

P_A is the sum of the thermodynamic probabilities, see eq 2, p 902, of the four postulated active conformations, and ϕ is the direction of the dipole moment of the substituted phenyl ring relative to the corresponding dipole for the most active analogue. Compounds **30** and **31** of Table I, p 901, had to be deleted in constructing this QSAR. The values of P_A and ϕ are available upon request from A.J.H.

All other results are valid, and the conclusions made do not need to be altered. However, an additional conclusion is that the dipole moment of the substituted ring is important to inhibition potency. This may indicate some specific electrostatic interactions between the ligand and the receptor.

Alan R. Katritzky,* Kenneth C. Caster,† Thomas H. Maren,* Curtis W. Conroy, and Amir Bar-Ilan: Synthesis and Physicochemical Properties of Thiadiazolo[3,2-*a*]pyrimidinesulfonamides and Thiadiazolo[3,2-*a*]-triazinesulfonamides as Candidates for Topically Effective Carbonic Anhydrase Inhibitors.

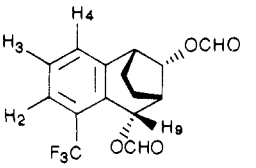
Page 2061. The intraocular pressure was not "measured in anesthetized rabbits" as stated but in non-anesthetized awake rabbits given a local anesthetic (0.25% proparacaine) on the cornea.

In the measurement of the rate constant (k_{in}) for transcorneal penetration in the rabbit eye, the concentration of compound applied to the artifically created corneal well (C_{out}) was not (as stated) taken as constant. C_{out} was actually measured at the start and end (10 min later) of drug exposure time, and the mean concentration was used for C_{out} in the calculation of k_{in} as shown in Table I. For

relatively lipid soluble compounds, the depletion of C_{out} was at most 2-fold.

Gary L. Grunewald,* Kimberly M. Markovich, and Daniel J. Sall: Binding Orientation of Amphetamine and Norfenfluramine Analogues in the Benzonorbornene and Benzobicyclo[3.2.1]octane Ring Systems at the Active Site of Phenylethanolamine *N*-Methyltransferase (PNMT).

Page 2191. In structures **41–44** and **51–55**, the stereochemistry of the oxygenated function at the benzylic position is incorrectly drawn. In all cases the stereochemistry should be represented with a dashed (rather than solid) line. For example, compound **41** should be as drawn below.



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Book Reviews

Hetero Diels–Alder Methodology in Organic Synthesis. Organic Chemistry, a Series of Monographs, Volume 47. Dale L. Boger and Steven N. Weinreb. Series Editor: Harry H. Wasserman. Academic Press Inc., Harcourt Brace Jovanovich, San Diego. 1987. x + 366 pp. 16 × 23 cm. ISBN 0-12-110860-0. $89.00.

The hetero Diels–Alder reaction has, in recent years, become firmly established as a strategy for the construction of complex natural products. The present volume is an important addition to this excellent series of monographs on organic chemistry and is written by two of the foremost advocates of this synthetic methodology.

The book is divided into 10 chapters, the first six of which deal with the use of various types of heterodienophiles. The remaining four chapters are concerned with the reactions of several classes of heterodienes. Throughout the work the emphasis is upon the practical significance of the hetero Diels–Alder reaction though in many cases this is of necessity due to the paucity of existing mechanistic information.

Many of the examples cited in this work are presented in tabular form, which includes such information as reaction conditions and yields as well as references to the original literature. This layout makes the book an ideal reference for the practicing chemist since it allows a rapid preliminary assessment of the value of the methodology for their own particular needs. The text is well supported by over 1000 references covering the literature through 1986.

This work succeeds well in its major aim of drawing the attention of organic chemists to the power of the hetero Diels–Alder reaction for stereoselective synthesis. It should, however, also suggest areas of fruitful research for the mechanistic organic chemist. The book should be included in the library of all academic and industrial institutions where synthetic organic chemistry is an integral endeavor.

Smith Kline & French Laboratories **John D. Elliott**
Philadelphia, Pennsylvania 19101

Chemical Research Faculties. An International Directory, 2nd Edition. Coordinated by Meg Marshall. American Chemical Society, Washington, D.C. 1988. xlvii + 689 pp. ISBN 0-8412-1017-9. $159.95.

This is the second edition of *Chemical Research Faculties*. The first edition (1984) derived from a need within the scientific community for current information about chemical colleagues throughout the world. The present edition details descriptions of areas of specialization and research conducted in 107 countries; it complements similar information on university faculties in the United States and Canada which is contained in the *ACS Directory of Graduate Research 1987*. This compilation derives from data collection initiated in December 1986 in which representatives from 149 countries were contacted. Listings are included for more than 11 500 individual faculty members, their field of interest, and their current research. *Chemical Research Faculties* also provides information on 72 chemical societies, including addresses, principal officers, publications, structures, and membership enrollments. The first 558 pages list faculties of various departments of chemistry in the countries included. The next 23 pages list corresponding chemical engineering societies. This is followed by 99 pages devoted to an Index of Research Subjects, and seven pages that present an Index of Institutions.

The book is one which provides invaluable information that should be available in all libraries, academic institutions, chemically oriented businesses, and chemical societies. The objective of the American Chemical Society in compiling this volume, i.e., to foster international communication to increase and improve scientific developments serving humanity, has been admirably achieved.

Staff

Neuromethods. 9. Neuronal Microenvironment. Edited by Alan A. Boulton, Glen B. Baker, and Wolfgang Walz. Humana Press, Clifton, NJ. 1988. xxvi + 732 pp. ISBN 0-89603-15-2. $94.50.

This latest volume in the *Neuromethods* series is directed toward a relatively new area of neuroscience, the neuronal microenvironment. It is based on the observation that 20% of the brain volume is extracellular space and is a functional compartment in itself. By virtue of its changes in electrolyte composition and volume it influences neuronal excitability and, indeed, many pathological processes. For example, stroke, eschemia, anoxia, and epilepsy involve dramatic changes in these factors. The 14 chapters in the book clearly describe information on the topic and latest techniques in ultrastructural and extracellular space, computer tomography and NMR, energy metabolism, ion and water shifts, ion-selective microelectrodes, voltammetric microsensors, brain slice preparations, cell cultures, techniques for assessing pathways and fluid dynamics in the blood–brain barrier and cerebral spinal fluid choroid plexus, cerebral spinal fluid system, arachnoid membrane, fluid compartment analysis, metabolic activity, patch clamp methods, acid–base balance, and calcium, magnesium, and hydrogen ion concentrations.

This is the first book dedicated to methodological approach for the study of the "neuronal microenvironment". It will serve as an important source of information to neuroscientists planning to initiate research in this promising, new, and rapidly developing area.

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