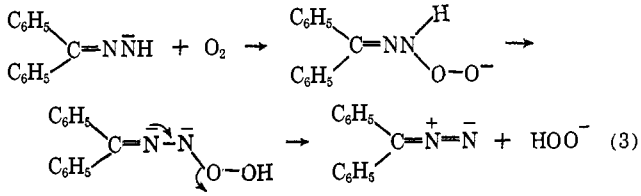
hydroperoxide anion[4] as shown in eq 3. The initial



attack is similar to that suggested for the oxidation of Grignard reagents by oxygen.[5]

(4) H. E. Zimmerman and D. H. Paskovich, *J. Am. Chem. Soc.*, **86**, 2149 (1964), footnote 12.
(5) C. Walling and S. A. Buckler, *ibid.*, **75**, 4372 (1953).

The interesting possibilities suggested by this novel reaction are under active investigation in our laboratories.

Acknowledgment. The generous support of this work by the National Institutes of Health under Grant GM 13689-01 is hereby acknowledged with deep appreciation.

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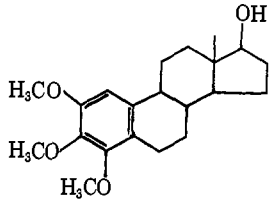
Additions and Corrections

A Steroidal Analgesic [*J. Am. Chem. Soc.*, **88,** 856 (1966)]. By LEONARD R. AXELROD and P. NARASIMHA RAO, Southwest Foundation for Research and Education, San Antonio, Texas, and DAVID H. BAEDER, Mallinckrodt Chemical Works, St. Louis, Missouri.

In the above publication, the synthesis of a new class of compounds having poly(lower alkoxy)estrane structures was reported. In a subsequent publication [L. R. Axelrod and D. H. Baeder, *Proc. Soc. Exptl. Biol. Med.*, **121,** 1184 (1966)], analgesic activity of one of these compounds was compared with that of some clinically active standard analgesics. Based on the findings of this investigation, the compound, MP-2001, *d*-2,3,4-trimethoxyestra-1,3,5(10)-trien-17β-ol



was reported to be more potent than morphine. More recently, laboratory testing of poly(alkoxy)estratrienes yielded results which indicated that the compounds were devoid of pharmacologic activity [D. R. Van Deripe, G. B. Hoey, W. R. Teeters, and T. W. Tusing, *J. Am. Chem. Soc.*, **88,** 5365 (1966)].

Since the pharmacologic evaluation of these compounds for the above-cited studies was not conducted in our laboratories, it was decided to reevaluate MP-2001 for analgesic activity using morphine and meperidine as comparison standards.

The procedures used were the tail-flick test in rats [F. E. D'Amour and D. L. Smith, *J. Pharmacol.*, **72,** 74 (1941)] and a variation of the titration method [B. Weiss and V. G. Laties, *Science*, **125,** 1575 (1958)] in a cynomolgous monkey. Our experience with the tail-flick technique revealed the necessity for rigid control of several critical variables to prevent false positives in the use of this test. We have discussed this elsewhere in detail [I. Geller and L. R. Axelrod, presented at the International Symposium on Pain, Paris, France, April 11–13, 1967]. These variables include ambient temperature, pretraining of animals, and sudden changes in exteroceptive stimuli. The titration method involves the periodic delivery to an animal of electric shocks of successively increasing intensities. In our procedure, the monkey was able to reduce the shock intensity to zero by pressing a lever. After a period of training, resets to zero generally occurred at the same shock level throughout a 6-hr experimental session.

Morphine and meperidine were prepared in water and MP-2001 was prepared in propylene glycol. The drugs were administered intraabdominally to the rats and intravenously to the monkey. Morphine and meperidine were both active in the tail-flick test, yielding AD_{50} values of 3.5 and 10.6 mg/kg, respectively. MP-2001, in a dose range of 1.0 and 16.0 mg/kg, showed no activity in this test. In the titration test, following intravenous administrations of morphine at 2.0 and 3.0 mg/kg and meperidine at 12.5 mg/kg, resets of shock levels to zero occurred at intensities above control values. The monkey tolerated higher shock intensities under morphine and meperidine. Intravenous administrations of MP-2001 at 5 and 10 mg/kg were ineffective in this test.

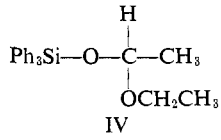
Electron Spin Resonance Studies of Substituent Effects. Correlations with σ Constants [*J. Am. Chem. Soc.*, **88,** 2065 (1966)]. By E. THOMAS STROM, Mobil Research and Development Corp., Field Research Laboratory, Dallas, Texas 75221.

In calculating the ρ values given in the communication, the coordinates were inadvertently reversed so the values cited are really the reciprocals of the slopes. Even if the ρ values had been calculated correctly, they would have units of gauss and would be meaningless in comparing the sensitivity of the hyperfine splitting constants to substituent. If the ratio $A^{H}_{sub}/A^{H}_{unsub}$ is plotted *vs.* σ, however, the slope will be unitless and its value will be a measure of the sensitivity of the system

to substituent. The ρ values derived in this manner are -0.343, -0.168, and -0.066, respectively, for 1-phenyl-1,2-propanesemidiones, nitrobenzene anion radicals (ref 1), and phenyl *t*-butyl nitroxides (ref 2).

The Photochemistry of Silyl Ketones in Alcohol [*J. Am. Chem. Soc.*, **89**, 454 (1967)]. By A. G. BROOK and J. M. DUFF, Department of Chemistry, University of Toronto, Toronto 5, Canada.

Formula IV on page 455 should be



IV

The Ionic Decomposition of 2-Substituted 2-Propyl *p*-Nitroperbenzoates. Migration to Electron-Deficient Oxygen and Anchimeric Acceleration of Peroxide-Bond Heterolysis [*J. Am. Chem. Soc.*, **89**, 1661 (1967)]. By E. HEDAYA and S. WINSTEIN, Union Carbide Research Institute, Tarrytown, New York, and the Department of Chemistry, University of California, Los Angeles, California.

On page 1670, in the description of the preparation of 1-phenyl-2-methyl-2-propyl hydroperoxide, the first sentence should read: "Dimethylbenzylcarbinol (6 g) was combined with 30 ml of 90% hydrogen peroxide acidified with 12 drops of concentrated sulfuric acid."

The incorrect procedure is hazardous. Professor W. Adam has informed us that a violent and damaging explosion occurred when concentrated sulfuric acid was added to the mixture of alcohol and 90% hydrogen peroxide. In our hands, no explosions occurred when the alcohol was added to acidified 90% hydrogen peroxide. Nevertheless, all safety precautions in this preparation and similar ones should be routinely taken.

The Chemistry of Methylnorbornyl Cations. V. Solvent Capture and Hydride Shift in the 3-*endo*-Methyl Series [*J. Am. Chem. Soc.*, **89**, 2581 (1967)]. By JEROME A. BERSON, ROBERT G. BERGMAN, JAMES H. HAMMONS, and ARTHUR W. MCROWE, Departments of Chemistry, University of Wisconsin, Madison, Wisconsin, and University of Southern California, Los Angeles, California.

On page 2589, eq 12 can be factored and reduces to eq 11, as has been pointed out to us by Dr. Frank B. Miles. The value $k_{SOH}/k_H = 2.88$ derived on the assumption $k_H = k_T$ therefore applies also when $k_H \neq k_T$. This conclusion has been reached independently by Dr. Clair J. Collins. The other results of the Appendix remain unchanged.

Anomalous Behavior of 3-*endo*-Hydroxy-3-*exo*-phenyl-2-*endo*-norbornylamine during Deamination [*J. Am. Chem. Soc.*, **89**, 3940 (1967)]. By CLAIR J. COLLINS, VERNON F. RAAEN, BEN M. BENJAMIN, and IRVING T. GLOVER, Chemistry Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee.

On page 3941, column 1, line 12, "water" should read "acetic acid–sodium acetate"; in line 30, "σ-hydrogen" should read "*o*-hydrogen."

Book Reviews

The Acridines. Their Preparation, Physical, Chemical, and Biological Properties and Uses. Second Edition. By ADRIEN ALBERT, D.Sc. (London), Ph.D. Medicine (London), B.Sc. (Sydney), F.R.I.C., Professor of Medical Chemistry, John Curtin School of Medical Research, The Australian National University, Camberra. Fellow of the Australian Academy of Science. St. Martin's Press Inc., 175 Fifth Ave., New York, N. Y. 1966. xii + 604 pp. 15.5 × 23.5 cm. $32.50.

The appearance of the first edition of "The Acridines" some 15 years ago represented the first comprehensive treatment of this group of compounds. In the meantime Professor Albert has continued his intense interest in this field which culminates with the production of a second edition, a volume of classic proportions. It contains a wealth of information of interest to such varied disciplines as those of the organic chemist, the industrial chemist, the medicinal chemist, the pharmacist, and the clinician. During this period many developments both in the chemistry and in the application of acridines have occurred. The magnitude of this trend may be illustrated by the fact that world production of acridine drugs has increased to over 500 tons a year and by the introduction of the "Monastral" pigments.

The book is divided into five parts, each of which is a rich lode of information. Part 1 deals with the general organic chemistry of the acridines—their interconversions and preparations. A number of detailed preparative procedures, all of which have been checked in Albert's laboratory, are a distinguishing feature as is a critical discussion on the choice of preferred synthetic methods not only for the final acridines but for many of the intermediates as well.

Part 2 covers the physical properties in depth including surface activity, association, and ionization, characteristics which play a major role in determining bacteriostatic effectiveness, as well as dipole moments, and spectra including fluorescence and phosphorescence. Relatively few of these data were available when the first edition of the book was written. This part will appeal to the physical organic chemist interested in correlation of properties with electronic distribution.

The chemical properties of acridines and their functional derivatives comprise Part 3. Again many checked synthetic procedures for specific compounds are presented. Throughout the section detailed monographs dealing with groups of especial interest, *e.g.*, drugs, dyes, etc., are scattered. Included are Pharmacopoeia specifications and several formulations.

Part 4, comprising some 120 pages, is devoted to biological properties and uses of the acridines as therapeutic agents. The historical approach to the development of this subject results in a thoroughly readable narrative. Clinical aspects of therapeutic uses are gone into in considerable detail, and the relationship between biological properties and physical and chemical properties is emphasized.

The final part deals with applications of acridines as dyestuffs and pigments as well as other miscellaneous uses such as analytical reagents, photographic applications, energy cells, industrial disinfection, and preservation.

Throughout the volume numerous and voluminous tables are scattered with some 2000 literature citations so that one will have no difficulty in running down the literature on a given compound. The literature has been surveyed through September 1965, which is no small accomplishment in a book of this size. The style is free and fluid and the book is remarkably readable. Typography is excellent. Some redundancies between the various sections might have been eliminated with some saving in space. However, this is a minor criticism in view of the definitive and critical treatment of the over-all subject. Professor Albert is to be congratulated for providing an outstanding treatise.

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