effected methylation of the pyrazole nitrogen also (**25**): *m/e* 476 (M^+), 296, 181.

Benzhydryl 3-(*N*-Methyl-5-methoxycarbonylpyrazol-3-yl)-7β-(2-thienylacetamido)-3-cephem-4-carboxylate (26). Compound **23** (53 mg, 10^{-4} mol) in 3 ml of CH_2Cl_2 was treated with excess CH_2N_2 in ether. After 3 h the solvent was removed to give a quantitative yield of product: mp 206–208°; ir (film) 3320, 1790, 1755, 1675 cm^{-1}; NMR ($CDCl_3$) δ 3.53 (d, 1 H, *J* = 18 Hz), 3.90 (d, 1 H, *J* = 18 Hz), 3.80 (s, 2 H), 3.87 (s, 6 H), 5.03 (d, 1 H, *J* = 5 Hz), 5.90 (dd, 1 H, *J* = 5, 8 Hz), 6.47 (d, 1 H, *J* = 8 Hz), 6.54 (s, 1 H), 7.0–7.5 (m, 14 H); *m/e* 628 (M^+), 448, 417. Conversion with TFA–anisole to the free acid **27** followed by treatment with CH_2N_2 gave **25** with the mass spectrum identical with that of the previous sample.

Benzhydryl 3-(5-Ethoxycarbonylpyrazolin-3-yl)-7β-(2-thienylacetamido)-3-cephem-4-carboxylate (28). A solution of compound **22** (106 mg, 2.0×10^{-4} mol) and ethyl acrylate (20 μl, 2×10^{-4} mol) in CH_2Cl_2 was refluxed 12 h, evaporated, and chromatographed by PLC on silica gel with EtOAc–$CHCl_3$ (1:1) to give 46 mg of product (36%) at R_f 0.65: ir (film) 3300, 1780, 1730, 1680 cm^{-1}; NMR ($CDCl_3$) δ 1.1–1.6 (m, 5 H), 3.42 (br s, 2 H), 3.81 (s, 2 H), 4.0–4.6 (m, 4 H), 4.98 (d, 1 H, *J* = 4 Hz), 5.85 (dd, 1 H, *J* = 4, 9 Hz), 6.70 (d, 1 H, *J* = 9 Hz), 6.9–7.6 (m, 14 H). The free acid was obtained with TFA–anisole.

Benzhydryl 3-(4,5-Diethoxycarbonylpyrazol-3-yl)-7β-(2-thienylacetamido)-3-cephem-4-carboxylate (29). A solution of **22** (42 mg, 8.0×10^{-5} mol) and diethyl acetylenedicarboxylate (12.4 μg, 8.0×10^{-5} mol) in CH_2Cl_2 was stirred at room temperature for 2 h, evaporated, and chromatographed by PLC on silica gel with $CHCl_3$–EtOAc (1:1) to give 20 mg of product (36%): *m/e* 700 (M^+).

Benzhydryl 3-(5-Trifluoromethyl-1,2,3-triazol-4-yl)-7β-(2-thienylacetamido)-3-cephem-4-carboxylate (30). Trifluoroacetonitrile was slowly bubbled into a solution of **22** (106 mg, 2.0×10^{-4} mol) in 50 ml of acetonitrile for 3 h. The mixture was stoppered for 5 days. The solvent was then removed and the resulting oil chromatographed by PLC on silica gel with EtOAc–$CHCl_3$ (1:1) to give 62 mg of product (50%): *m/e* 625 (M^+).

Benzhydryl 3-(Oxonitrilomethyl)-7β-(2-thienylacetamido)-3-cephem-4-carboxylate (31). To a stirred suspension of compound **2** (106.9 mg, 2.0×10^{-4} mol) in CH_2Cl_2 at −78° was added 60 μl of triethylamine (9×10^{-4} mol). After 5 min a solution of 96 mg of lead tetraacetate (2.0×10^{-4} mol) in 5 ml of CH_2Cl_2 was added dropwise. The reaction mixture was allowed to warm to 0°, poured into 100 ml of ice water, and extracted with 5 × 15 ml of ether. The ether solution was dried with $MgSO_4$, filtered, evaporated, and chromatographed by PLC on silica gel with benzene–THF (5:1), developing for only 15 min, to give 35 mg of product: 33%; ir (film) 3220, 2285, 1790, 1730, 1675 cm^{-1}; NMR ($CDCl_3$) δ 3.38 (d, 1 H, *J* = 7 Hz), 3.78 (s, 2 H), 4.02 (d, 1 H, *J* = 7 Hz), 4.92 (d, 1 H, *J* = 5 Hz), 6.00 (dd, 1 H, *J* = 5, 8 Hz), 6.9–7.6 (m, 15 H).

Benzhydryl 3-(5-Phenylisoxazol-3-yl)-7β-(2-thienylacetamido)-3-cephem-4-carboxylate (32). A solution of **31** (106 mg, 2.0×10^{-4} mol) in 1 ml of phenylacetylene was kept 30 min at room temperature and then chromatographed by PLC on silica gel with benzene–THF (5:1), affording 36 mg of product, 28%, at R_f 0.70: ir (film) 3300, 1790, 1740, 1675 cm^{-1}; NMR ($CDCl_3$) δ 3.18 (d, 1 H, *J* = 18 Hz), 3.80 (s, 2 H), 3.97 (d, 1 H, *J* = 18 Hz), 4.97 (d, 1 H, *J* = 5 Hz), 5.95 (dd, 1 H, *J* = 5, 8 Hz), 6.54 (d, 1 H, *J* = 8 Hz), 6.9–7.5 (m, 20 H). Cleavage to the acid **33** followed by CH_2N_2 gave methyl ester **34**: *m/e* 481 (M^+), 422, 301, 181.

Acknowledgment. We thank Dr. E. H. Thiele for the antibacterial measurements.

References and Notes

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Book Reviews

Advances in Chromatography. Volume 12. Edited by J. C. Giddings, E. Grushka, R. A. Keller, and J. Cazes. Marcel Dekker, New York, N.Y. 1975. xiv + 278 pp. 15 × 23.5 cm. $22.50.

This book, the twelfth volume in the series, consists of seven chapters covering a wide range of chromatography topics. Anyone, except the most serious chromatographer, will find only a few chapters of this book (and previous volumes) to be of interest. In this particular book, readers of Journal of Medicinal Chemistry will probably find Chapter 1, "The Use of High Pressure Liquid Chromatography in Pharmacology and Toxicology", and Chapter 3, "Practical Methods of High Speed Liquid Chromatography", to be most useful. These are the first two chapters which truly describe modern high-pressure liquid chromatography to appear in the Advances in Chromatography Series.

Dr. P. R. Brown in Chapter 1 "whets the appetite" by showing many examples of how liquid chromatography already has analyzed mixtures of physiological fluids, cell extracts, drugs, and many other biologically active compounds. Since the writing of this chapter the technology of high-pressure liquid chromatography has advanced so that in 1975 even faster analyses can be obtained or more complex samples can be resolved. Two types of analyses described by Dr. Brown are carbohydrates in urine and nucleotides in whole blood.

Chapter 3, "Practical Methods of High Speed Liquid Chromatography", by G. J. Fallick is a good follow up to Chapter 1. If Chapter 1 gets your attention that high-pressure liquid chromatography could be used in your research, then Chapter 3 will give you a basic introduction to the jargon of the technique and how to select conditions (column packing material, solvents, etc.). The chapter also describes the technique of scaling analytical liquid chromatographic analyses up to preparing pure compounds in the few hundred milligram range.

The other five chapters are all very well written but will have only limited interest to readers of this Journal. Chapter 2 reviews chromatographic separations of cellulose and its derivatives; Chapter 4 discusses measuring diffusion coefficients by gas chromatography; Chapter 5 gives examples of GC analyses of polychlorinated biphenyls; Chapter 6 presents high-performance

electrometer systems for GC; and Chapter 7 describes steam carrier GC.

This reviewer feels the series might have an overall greater appeal if all chapters in a particular volume related to a specific applications area or a specific technique. I do not believe most medicinal chemists would chose to own this book unless they were very interested in having two very well written chapters on high-pressure liquid chromatography handy.

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Topics in Current Chemistry. Fortschritte der chemischen Forschung. Medicinal Chemistry. Volume 52. Edited by A. Davidson, M. J. S. Dewar, K. Hafner, E. Heilbronner, U. Hofmann, J. M. Lehn, K. Niedenzu, Kl. Schäfer, and G. Wittig. Springer-Verlag, Berlin, Heidelberg, New York. 1974. iii + 233 pp. 15.5 × 23.5 cm. $25.50.

This volume contains six chapters entitled "Design of Bioactive Compounds" by E. J. Ariens and A.-M. Simonis (62 pages, 172 references), "Antimetabolites: Molecular Design and Mode of Action" by T. J. Bardos (37 pages, 133 references), "Molecular Approaches for Designing Antiviral and Antitumor Compounds" by P. Chandra (43 pages, 63 references), "Alkylating Agents" by T. A. Connors (32 pages, 97 references), "Synthetic Interferon Inducers" by E. De Clercq (26 pages, 202 references), and "Synthesis and Properties of Some New NAD^+ Analogues" by C. Woenckhaus (24 pages, 66 references). Most chapters are referenced into 1973.

The chapter by Ariens and Simonis contains a wealth of information which should be read by both the beginner and the experienced investigator interested in designing compounds having selective activity in either animals, plants, or insects. Although experienced medicinal chemists will be familiar with most of the biochemical and/or metabolic concepts used in drug design which are discussed by these authors, the chapter is so nicely organized that even the experienced individual likely will see new insights applicable to the specific research problem on which he or she is working. This chapter, which emphasizes the pharmacodynamic, pharmacokinetic, transport, and depot action of drugs and their design from a biochemical point of view, is followed by an equally well-written and biochemically oriented chapter on antimetabolites by Bardos. In his section, Bardos discusses classical, nonclassical, dual, and macromolecular antimetabolites. The chapter is rather complete and review articles are referenced for additional information. The chapter by Chandra, which follows Bardos' section, also contains much useful information on distamycin A, daunomycin and its derivatives, tilorone, and modified nucleic acids. Various binding studies to DNA, structure–activity studies, and the results of many biological investigations are summarized in both chapters.

Next, Connors discusses the various alkylating agents including their biological properties and mechanisms of alkylation. Difunctional alkylating compounds, selectivity of action, development of resistance, and clinically useful drugs are also considered. In addition to discussions of the classic nitrogen mustards the triazenes, nitrosoureas, platinum compounds, mitomycin C, DON, and procarbazine are considered along with what is generally known about their mechanism of action. A short section on carcinogenic alkylating agents is included. Although much of this chapter may be found in other works this section represents a well-written concise review of the subject.

De Clercq's discussion of interferon inducers only includes a discussion of synthetic materials (polycarboxylates, polynucleotides, and a short section on low-molecular-weight compounds). The chapter is well organized and interesting to read. A section on the mechanism of interferon production by cells exposed to the synthetic inducers is included. Woenckhaus' concluding chapter considers new NAD^+ analogues in terms of coenzyme–enzyme complexes, coenzyme analogs, the ribose moiety in the coenzyme molecule, and modification of the amino acids at the active center. Like the others, this chapter is also interesting and well written.

It is clear that the authors of all six chapters have given considerable thought to their preparation. This monograph could serve as an excellent source of lecture material for both graduate and undergraduate courses in medicinal chemistry and chemical pharmacology as well as a source of information for predoctoral cumulative examinations. The book is recommended reading for all medicinal chemistry students, faculty, and researching investigators whether or not they are pursuing the specific areas discussed.

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Antibiotics. III. Mechanism of Action of Antimicrobial and Antitumor Agents. Edited by J. W. Corcoran and F. E. Hahn. Springer-Verlag, New York, N.Y. 1975. 742 pp. $77.10.

The antibiotic literature is voluminous and widely scattered even by medicinal chemistry standards. Periodic reviews on various aspects of the subject by experts are not a luxury but rather a necessity for those who have a serious interest in our phase of the subject and a perceived need for an understanding of what others are doing in related areas. For this reason the appearance of Volume III of the Springer series was eagerly anticipated. The first two volumes of this excellent series, under different editorship, have been widely used and quoted and, even though Volume I, which appeared in 1967, also dealt with mode of action, enormous strides have been made in the intervening years and a new volume is welcome. Unfortunately, the price ($77.10) is well beyond what the average medicinal chemist can afford, but no company or university library should be without a copy, and medicinal chemists will profit from browsing here for background and ideas. Forty-six reviews, mainly critical, are included and the volume is divided into three main sections: Interference with Nucleic Acid Biosynthesis; Interference with Protein Biosynthesis; and Interference with Cell Wall/Membrane Biosynthesis, Specific Enzyme Systems and Unknown Mode of Action. The individual chapters read very well, are written in the main by authors active in research in the area they review, and, for a multiauthored tome of this magnitude, are remarkably up to date. A check of the references shows that most of the articles' coverage ends with 1972, with an occasional reference to 1973 and even, in some cases, 1974. The text is surprisingly free from errors (nitpickers may search for a typo on pp 101, 579, etc.) and the quality of the reproduction and paper is excellent, although the binding is inferior to Volumes I and II. Liberal use of formulas and a color photograph on p 157 illustrating the intercalation of ethidium into DNA are useful.

The subject coverage is broad including, for example, bleomycin, camptothecin, daunomycin–adriamycin, nalidixic acid, acridines, rifamycins, thiaxanthenes, trimethoprim, althiomycin, emetine, fusidic acid, gougerotin, mickamycin, thiostreptone, berberine, irehdiamine, INH, sideromycins, vancomycin, and the classical antibacterial antibiotics, etc. One can, however, question the omission of some of ones favorites which are still the subject of lively research, such as the penicillin–cephalosporins and the tetracyclines. Grouping streptomycin, dihydrostreptomycin, and gentamicin and separating these from "aminoglycoside antibiotics" seems curious, but the chapters are, nonetheless, well written. The chapter by Tanaka on the aminoglycosides and that of Vasquez on the macrolides and Burchall on trimethoprim seem to me to be especially well written and thorough.

In a field moving as fast as this one, a Volume IV will soon be required and it is hoped that the high quality of Volume III will be maintained. It is, however, feared that the price of Volume IV will penetrate into three figures.

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The *Catharanthus* Alkaloids. Edited by William I. Taylor and Norman R. Farnsworth. Marcel Dekker, New York, N.Y. vii + 323 pp. 15 × 23 cm. $29.50.

The *Catharanthus* alkaloids hold a unique position among indole alkaloids because of their chemical diversity and complexity and because of the clinical importance of vinblastine and vincristine as antitumor agents. In this role, these compounds have

achieved widespread recognition with exceptional rapidity, despite the fact that very little is yet known of their mechanisms of action on the molecular level.

For these reasons, a book giving a wide overview of scientific work on *Catharanthus* alkaloids is needed, since workers from the many different disciplines involved need to be acquainted with work of their colleagues in other fields. Such a book will also serve to illuminate the background again for specialists as well as to introduce the field to students. This book, which answers these needs, has been edited by two distinguished authorities in the field. The contributors are all well-known workers in this and related areas.

The book begins with a botanical synopsis of the genus *Catharanthus* (William T. Stearn), necessary in view of the terminological confusion with the genus *Vinca* in the earlier literature, and interesting to the phytochemist and alkaloid chemist. *Catharanthus roseus*, from which vinblastine and vincristine are obtained commercially, is reviewed from the phytochemical and pharmacological viewpoints by Gordon H. Svoboda and David A. Blake. The fascinating story of the discovery of the antitumor activity of *C. roseus* is here combined with a summary of the alkaloidal constituents of this chemical cornucopia. The next chapter (M. Tin-Wa and Norman R. Farnsworth) reviews work on other *Catharanthus* species. Both these chapters will be of interest to all those interested in procedures for extraction of alkaloids from plants. The structure elucidation and chemistry of the bisindole alkaloids are then reviewed by Donald J. Abraham. The summarized chemical information is interleaved with data derived from mass spectrometric and x-ray crystallographic work.

If these first four chapters can be regarded as being concerned with botany, phytochemistry, and molecular structures, the latter four deal with the "dynamic" biology of the plant and its alkaloids. Ronald J. Parry puts the biosynthesis of *Catharanthus* alkaloids in general perspective with the rest of the indole alkaloid group, and David P. Carew reviews the difficult and fairly early initiated studies of *C. roseus* in tissue culture. The final two chapters discuss the biochemistry of the bisindole alkaloids (William A. Creasey) and clinical aspects of their action as antitumor agents (R. C. DeConti and William A. Creasey). The mechanism of action of vinblastine and vincristine has been investigated biochemically (inhibition of nucleic acids) and is manifested by fascinating cytological effects on cellular microtubules; but clearly the full story is yet to come. The chapter on clinical aspects of the action of vinblastine and vincristine will be interesting and informative to all workers on these compounds, whether themselves clinicians or not.

This is a valuable book, despite the lag sometimes seen between the preparation of some chapters and the date of publication, and will be interesting to a wide variety of scientists. The price seems somewhat high for a book of this length prepared by direct reproduction.

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History of Coca—"the Divine Plant" of the Incas. By W. Golden Mortimer. And/Or Press, San Francisco, Calif. 1974. xxxi + 576 pp. 14 × 22 cm. $15.00 hardbound, $8.50 softbound.

This is a reprint of Mortimer's now classic work on coca first published at the turn of the century. Its appearance is most timely coinciding, by all accounts in the recent press, with a resurgence of the popular hedonistic use of cocaine and its consequent illegal importation and distribution.

The first half of the book (Chapters I–VII) details the history of the Incan empire, its religion, art, economy, and politics in all of which *Erythroxylon coca* was as much a part of cultural life as other "sacred" plants have been, and still are, to many of the world's peoples. No wonder, then, that the repressive measures of the Conquest failed completely to eradicate the use of coca among Andean communities but led, eventually, to its introduction into European medicine.

The latter half (Chapters VIII–XVI) of the work sets the stage for the controversy which has surrounded the plant and its alkaloids since the publication of the effects of cocaine by Koller, Freud, and others late in the 19th century. Quite aside from its use as a local anesthetic in which it was certainly replaced by more effective synthetics, cocaine and coca preparations were used for a variety of medical applications many of which, undoubtedly, would be considered "quaint" by the modern physician. Like any new drugs they had their protagonists and antagonists among the medical men of the time and certainly Mortimer, a respected New York physician, must be numbered among the former. He and his colleagues used only coca extracts, or the leaf itself, by oral administration for "the qualities of coca are not fully represented by any one of its alkaloids thus far isolated".

This fascinating history raises a number of questions; it should suggest a number of modern studies on the botany, chemistry, and pharmacology of coca, some of which, after a lapse of 70 years, are actually underway. The bibliography contains 570 references to the older literature.

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Poisonous Plants of Australia. By Selwyn L. Everist. Angus and Robertson Publishers, Sydney, Australia. 1974. xvi + 684 pp. 15.5 × 24.5 cm. $45.00.

The preface identifies this book as a description of "the plants in Australia that are definitely known to be capable of poisoning livestock or man". On reading further, two things become clear: in deference to the major Australian industries of meat and wool, emphasis is placed on toxicity to livestock; the plant species described include not only those native to Australia but also introduced species as well. Thus in some sections, descriptions are reminiscent of Kingsbury, Watt, and Breyer-Brandwijk and similar compendia which exist for other parts of the world.

A brief introductory section deals with general considerations: the economic importance of toxic plants, methods of investigation, factors affecting toxicity, notes on prevention and treatment, etc. The bulk of the descriptive material in the second section details the individual plant species, their toxic principles, where known, symptoms, prevention, and treatment. Three appendices and a comprehensive index give the reader access to the contents by way of geographical distribution, toxic symptoms, toxic principles, and botanical as well as common names. The volume is beautifully illustrated with 64 full-color plates, an equal number of black and white photographs, and 42 line drawings.

This book should have its major appeal for those involved in veterinary medicine or food production and for natural product chemists to whom simply the characterization of toxic principles of plants represents a challenge. For in spite of the recent progress in our abilities in this direction, there are still many species whose toxic constituents have not been identified.

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Drug Design. Volume VI. Edited by E. J. Ariens with 15 contributors. Academic Press, New York, N.Y. 1975. xvii and 364 pp. 15 × 23 cm. $39.50.

The latest volume in Ariens' series on Drug Design maintains, with high quality, the attempts of the previous volumes to present reviews on various aspects of medicinal chemistry designed to aid "practical approaches to the development of bioactive compounds". Although the intent of these reviews is not to be exhaustive, they do provide the reader with a full contemporary view of the topic discussed and should therefore succeed in their stated purpose.

The first chapter on diphenhydramine derivatives, by Harms,

Hespe, Nauta, Rekker, Timmerman, and deVries, presents the development of those classes of drugs which contain the benzhydryl moiety as a bioactive entity. A surprising number of drugs contain this moiety and represent several different classes of agents. Following a review of synthetic methods, the discussion centers on various "phases of manipulation". These include the classical approaches, by various synthetic substitutions, consideration of structural features, such as ether bond stability and base function, and correlation of ether bond stability and pK_a with linear free-energy parameters. Other physicochemical parameters are discussed in correlating structure and activity, including multiple regression analysis and influence of chirality. The roles of absorption, distribution, and biotransformation in relation to design are also considered, and this chapter is probably more closely related to the intent of the series than many of the others.

The remainder of the volume is taken up with reviews of a more conventional nature, but nonetheless highly informative, on the subjects of antiradiation agents, proteinase inhibitors, organ-imaging radiopharmaceuticals, x-ray contrast media, and formulation of agricultural pesticides. The chapter on the design of antiradiation agents, by Klayman and Copeland, presents a very good coverage of the more active compounds in each of the known classes of protective agents, with brief discussions of the nature of radiation damage, evaluation of potential agents, and theories of protection. This topic has not yet been treated successfully by correlation with physicochemical parameters, and in a review of this extent, none of the significant related aspects of radiation or thiol chemistry could be included.

The chapter on proteinase inhibitors by Okamoto and Hijikata covers quite adequately the development of agents with specificity toward proteinases with appropriate mention of the biological aspects involved. The same may be said of the chapters on organ-imaging radiopharmaceuticals, by Counsell and Ice, and x-ray contrast media, by Herms and Taenzer. Physical, chemical, and biological factors are considered in detail and make these chapters both highly informative and readable. The development of these agents, in the latter two chapters, is particularly well delineated and makes very interesting research stories.

The final chapter on agricultural pesticides, by Hartley, is concerned, of course, with the distribution, uptake, loss, and toxicity of the pesticides in plants. The purpose of this chapter, in a series on drug design, is to perhaps encourage cross fertilization of ideas with mammalian medicinal chemistry. The discussions on physical and chemical methods of formulation of these agents show many similarities with the methods of drug formulations, with perhaps greater utilization of prodrugs. This chapter is certainly not inappropriate for this series on drug design.

In his review of Volume I, Burger wondered "what rabbit Ariens will pull out of an almost emptied hat" to fill future volumes. Some very interesting subjects were pulled out of the hat in this volume, but the nature of the subjects discussed has required a more conventional treatment than was perhaps envisioned at the outset. The information presented here should be of great value to those concerned with these topics and should be found in every library devoted to medicinal chemistry. Some of these topics have not been treated in similar fashion elsewhere.

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Biosynthesis. Volume 3. Specialist Periodical Reports. By T. A. Geissman, Senior Reporter. The Chemical Society, Burlington House, London. 1975. viii + 293 pp. 14 × 22 cm. $11.00.

This volume, which reviews the literature of 1973, follows the format of previous volumes in the series. While it has been customary for authors to cite review articles which appeared in the year under consideration, a welcome innovation has been introduced in the chapter on biosynthesis of quinones in the form of brief summaries of earlier work so that the chapter can stand as a definitive modern treatment of the compound class. Chapters on terpenoids from C_5 to C_{40}, flavonoid polyphenols, alkaloids, and the physical methods used to study the biosynthesis of these compounds complete the volume.

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Corrections

1976, Volume 19

D. B. Rusterholz, C. F. Barfknecht, and J. A. Clemens: Ergoline Congeners as Potential Inhibitors of Prolactin Release. 2.

Page 101. In the final page makeup, some lines were misplaced in Results and Discussion, and the section in full should read as follows.

Results and Discussion

The results of the prolactin release inhioition assay are shown in Table I. The standard drugs ergocornine and apomorphine inhibited prolactin secretion by 60 and 29% at dosages of 10 μg/rat and 1 mg/rat, respectively. The drug, "M-7" (**14**), which has been shown to be a potent dopamine agonist,[23] is found to have a strong inhibitory action in this assay, thereby adding further support to the contention that inhibition of prolactin release results from dopaminergic agonism. The test compounds **4** and **6** have previously been shown to inhibit prolactin secretion in vitro when used in high concentrations.[1] In this assay **4** was relatively inactive, while **6** produced a 24% inhibition, which has only borderline significance at this dose level, but may exhibit a significant effect at higher doses. In the aminotetralin series **7–10**, methoxy substituents on the aromatic ring did not produce active compounds. However, hydroxy substituents did appear to confer activity to the aminotetralin structure when the 2-amino group was tertiary. The dramatic increase in activity which occurs when going from the secondary amine **12** to the tertiary amine **13** emphasizes the importance of the tertiary amine to activity in these agents. The structural similarity between **13** and **14** strongly suggests that **13** is a dopaminergic agonist as well. We are now involved in the confirmation of dopaminergic activity in **13** and other compounds.