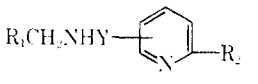
TABLE I

ω-N-(SUBSTITUTED BENZYL)AMINOALKYLPYRIDINES



No	R_1	Y	Position in the pyridine ring	R_2	Mp, °C	Formula[a]
1	3′,4′-$(CH_3O)_2C_6H_3$	CH_2	2	H	180–182	$C_{15}H_{18}N_2O_2 \cdot 2HCl$
2	3′,4′-$(CH_3O)_2C_6H_3$	CH_2	3	H	186–188	$C_{15}H_{18}N_2O_2 \cdot 2HCl$
3	3′,4′-$(CH_3O)_2C_6H_3$	CH_2	4	H	175–178	$C_{15}H_{18}N_2O_2 \cdot 2HCl$
4	3′,4′-$(CH_3O)_2C_6H_3$	CH_2	2	CH_3	153–155	$C_{16}H_{20}N_2O_2 \cdot 2HCl$
5	C_6H_5	$(CH_2)_2$	2	H	140–142	$C_{14}H_{16}N_2 \cdot 2HCl$
6	4′-HOC_6H_4	$(CH_2)_2$	2	H	97–99	$C_{14}H_{16}N_2O \cdot 2HCl$
7	2′-HOC_6H_4	$(CH_2)_2$	2	H	176–178	$C_{14}H_{16}N_2O \cdot 2HCl$
8	4′-$CH_3OC_6H_4$	$(CH_2)_2$	2	H	98–100	$C_{15}H_{18}N_2O \cdot 2HCl$
9	4′-$C_2H_5OC_6H_4$	$(CH_2)_2$	2	H	145–147	$C_{18}H_{20}N_2O \cdot 2HCl$
10	3′-CH_3O-4′-OHC_6H_3	$(CH_2)_2$	2	H	175–177	$C_{15}H_{18}N_2O_2 \cdot 2HCl$
11	3′,4′-$(CH_3O)_2C_6H_3$	$(CH_2)_2$	2	H	169–171	$C_{16}H_{20}N_2O_2 \cdot 2HCl$
12	3′-CH_3O-4′-$C_2H_5OC_6H_3$	$(CH_2)_2$	2	H	146–148	$C_{17}H_{22}N_2O_2 \cdot 2HCl$
13	3′,4′-$(OCH_2O)C_6H_3$	$(CH_2)_2$	2	H	113–115	$C_{15}H_{16}N_2O_2 \cdot 2HCl$
14	3′,4′,5′-$(CH_3O)_3C_6H_2$	$(CH_2)_2$	2	H	160–162	$C_{17}H_{22}N_2O_3 \cdot 2HCl$
15	4′-$NO_2C_6H_4$	$(CH_2)_2$	2	H	230	$C_{14}H_{15}N_3O_2 \cdot 2HCl$
16	4′-$(CH_3)_2NC_6H_4$	$(CH_2)_2$	2	H	166–167	$C_{16}H_{21}N_3 \cdot 3HCl$
17	4′-ClC_6H_4	$(CH_2)_2$	2	H	170–172	$C_{14}H_{15}ClN_2 \cdot 2HCl$
18	2′,4′-$Cl_2C_6H_3$	$(CH_2)_2$	2	H	200–204	$C_{14}H_{14}Cl_2N_2 \cdot 2HCl$
19	2′-Furyl	$(CH_2)_2$	2	H	132–133	$C_{12}H_{14}N_2O \cdot 2HCl$

[a] All compounds showed a correct analysis for C, H, N, Cl.

base was dissolved in Me_2CO and treated with HCl–EtOH to give a crystalline dihydrochloride which was recrystallized from EtOH–Me_2CO.

Acknowledgment.—The biological data were obtained by Dr. Professor J. Méhes, Dr. L. Decsi, and Dr. M. Karmos. Mrs. M. Ott, Mrs. A. Halász, and Miss T. Huszár participated in the experiments as technical assistants. Thanks are expressed for their cooperation.

Synthesis of Some New N-*o*-Tolyl-N′-2-(substituted) Benzothiazolylguanidines

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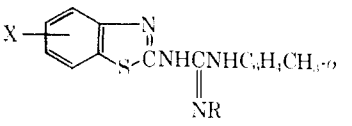
Certain substituted diguanides have shown antimalarial activities[1] which created interest in searching for other therapeutically useful members in this series and, in due course, led to the discovery of high antibacterial activity,[2] more commonly among a series of bisdiguanides. Biguanido derivatives[3,4] of diaryl sulfones and sulfides have been found to exhibit activity *in vitro* against *Mycobacterium tuberculosis*.

Recently, Bhargava, *et al.*,[5,6] have shown that hydrochlorides of several benzothiazolylguanidines are more active against gram-positive bacteria than against gram-negative ones. Some N-*m*- (or *p*-) tolyl-N′-2-(substituted)benzothiazolyl-N″-alkylguanidines have been found active against *M. tuberculosis* ($H_{37}Rv$).[7,8]

TABLE I

N-*o*-TOLYL-N′-2-(SUBSTITUTED) BENZOTHIAZOLYL-N″-ALKYLGUANIDINES[a]



No.	X	R	% yield	Mp, °C	Formula
1	H	CH_3	85	155	$C_{16}H_{16}N_4S$
2	4-Me	CH_3	80	119	$C_{17}H_{18}N_4S$
3	5-Me	CH_3	85	170	$C_{17}H_{18}N_4S$
4	6-Me	CH_3	90	184	$C_{17}H_{18}N_4S$
5	4-Cl	CH_3	70	198	$C_{16}H_{15}ClN_4S$
6	5-Cl	CH_3	75	220	$C_{16}H_{15}ClN_4S$
7	6-Cl	CH_3	85	130	$C_{16}H_{15}ClN_4S$
8	4-OMe	CH_3	60	169	$C_{17}H_{18}N_4OS$
9	6-OEt	CH_3	75	170	$C_{18}H_{20}N_4OS$
10	H	C_2H_5	85	195	$C_{17}H_{18}N_4S$
11	4-Me	C_2H_5	50	199	$C_{18}H_{20}N_4S$
12	5-Me	C_2H_5	45	135	$C_{18}H_{20}N_4S$
13	6-Me	C_2H_5	60	145	$C_{18}H_{20}N_4S$
14	4-Cl	C_2H_5	55	192	$C_{17}H_{17}ClN_4S$
15	6-Cl	C_2H_5	60	128	$C_{17}H_{17}ClN_4S$
16	4-OMe	C_2H_5	65	138	$C_{18}H_{20}N_4OS$
17	6-OMe	C_2H_5	70	108	$C_{18}H_{20}N_4OS$

[a] Crystallization solvent, EtOH. [b] All compounds were analyzed for N, S; analytical results were within ±0.3% of the calculated values.

(1) F. H. S. Curd and F. L. Rose, *J. Chem. Soc.*, 726 (1946).
(2) F. L. Rose and G. Swain, *ibid.*, 4422 (1956).
(3) B. N. Jayasimha, S. C. Bhattacharya, and P. C. Guha, *Current Sci.* (India), **20**, 158 (1951).
(4) M. Sirsi, B. N. Jayasimha, and J. R. Iyengar, *ibid.*, **20**, 237 (1951).
(5) P. N. Bhargava and K. S. Devi, *J. Indian Chem. Soc.*, **40**, 868 (1963).
(6) P. N. Bhargava and P. Ram, *Indian J. Chem.*, **4**, 95 (1966).
(7) P. N. Bhargava and R. Lakhan, *Agr. Biol. Chem.* (Tokyo), **32**, 1392 (1968).
(8) P. N. Bhargava and M. R. Chaurasia, *Current Sci.* (India), **37**, 347 (1968).

This led us to synthesize some new N-*o*-tolyl-N′-2-(substituted) benzothiazolyl-N″-alkylguanidines.

Experimental Section

N-*o*-Tolyl-N′-2-(substituted) benzothiazolylthiocarbamides were prepared by condensing 2-amino(substituted) benzothiazoles[9,10] with *o*-tolyl isothiocyanate.[11]

N-*o*-Tolyl-N′-2-(4-methyl)benzothiazolyl-N″-methylguanidine.—N-*o*-Tolyl-N′-2-(4-methyl)benzothiazolylthiocarbamide (3.5 g), yellow PbO (4.5 g), and $MeNH_2$–EtOH (25 ml) were heated in a glass autoclave on a water bath for 4 hr. After cooling, the product was boiled with EtOH (65 ml) and filtered while hot. The filtrate was concentrated and cooled when a crystalline product was obtained. It was recrystallized (EtOH) to yield white shining plates.

Similarly, other N-*o*-tolyl-N′-2-(substituted) benzothiazolyl-N″-alkylguanidines were prepared using $MeNH_2$–EtOH and $EtNH_2$–EtOH (see Table I).

(9) A. Hugershoff, *Ber.*, **36**, 3121 (1903).
(10) P. N. Bhargava and B. T. Baliga, *J. Indian Chem. Soc.*, **35**, 807 (1958).
(11) P. N. Bhargava and P. Ram, *Indian J. Appl. Chem.*, **24**, 181 (1961).

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Book Reviews

Steroid Hormone Analysis. Volume I. Edited by H. CARSTENSEN. Marcel Denker Inc., New York, N. Y. 1967. 493 pp. 22.8 × 15.0 cm.

This is the first volume of a two-volume work of ambitious proportions. It includes sections by various authors on isotopic-derivative labeling (^{35}S), ir and nmr spectroscopy, paper chromatography of steroids, estimation of testosterone, gas chromatography, and on steroid conjugates. For the most part each section is a review of the available literature in the field with, in most cases, a natural emphasis upon the methods devised or used by the authors themselves. The authors are to be commended for the thorough job that they have done in assembling the massive literature in this field, and the book is, for the most part, a valuable compilation for experts or semiexperts who are themselves working in this area. It is hard to assess its value to the nonexpert until the second volume will have appeared.

I found the two last chapters on gas chromatography and on the analysis and identification of steroid conjugates to be the most concise and useful in this book. Thus, the former condenses a large number of references to a convenient tabular form and discusses in down-to-earth terms the major practical problems that beset investigators in this field. It can be recommended to both the expert and the nonexpert as an excellent survey complementing other reviews of the last 6 or 7 years and adding more recent experience from the author's own laboratory. The chapter on steroid conjugates was timely in that a large amount of work has been done in this field since it was last reviewed comprehensively. Both chapters refer to useful theoretical considerations underlying the techniques they review while containing a useful selection of practical points for the beginner in these fields.

While the other chapters in this book contain much more material of great interest to the expert, they leave a very patchy impression. Most of them are much too long and there are many examples of sections which read like lists of quotations from the literature of the sort seen in many *Annual Reviews* volumes. The editor rightly wished to include material from biochemistry, physiology, and chemical pathology which would give the necessary background of information on the applications of the techniques discussed by the authors. However, the balance between this type of material and accounts of analytical techniques is extremely uneven, so that some sections are devoted effectively to reviewing literature on steroid biosynthesis and metabolism. These and other sections of the book are often marred by a prolix style, serious mistakes in English, and a form of cryptic reference to the literature which is of little value to the reader. In a discussion of the secretion of androgens by the adrenal cortex, for instance, we read on p 326, "Baulieu (*57*) has discussed why he thinks the presence of free dehydroepiandrosterone in human adrenal vein blood may be an artifact." No further discussion of this point is made in the text, and the information content of this sentence is effectively, "Get reference *57* out of the library and see what you think of it." On p 328 we read, "Short has discussed the physiological significance of weak androgens present in adrenal vein blood (*71*) and we concur fully with his conclusion. With dehydroepiandrosterone matters may be different (*71*)...." In the following discussion there is no further reference to Short or to his conclusion so that we are left with the impression that Short is obviously a good chap but that we had better get reference *71* out of the library if we are to find out why.

Similarly, Bojesen in the first chapter provides a number of original and stimulating discussions of the basic factors determining the precision and practicability of methods using radioactively labeled reagents. The discussion, however, is somewhat prolix and few, if any, clear guidelines emerge. It reads, in fact, rather like the unedited transcript of a first-class after-dinner dissertation which was cut short by the speaker being called to the telephone. Similarly the chapter on paper chromatography while giving a very comprehensive view of the techniques used in the author's laboratory, adds very little to the existing literature and, in fact, repeats a large amount of it at great length. While this chapter contains a number of items of interest to the expert, there is little that has not been discussed fully in the previous literature, and many of the statements and arguments are difficult to accept. Some of these can be rejected with confidence, and would be seriously misleading to newcomers to this field.

It is possible that the defects reviewed above may be remedied by the second volume when it appears, but one is left with the impression that this is not a book at all, but simply a collection of reviews. Perhaps this is a difficulty which will always be observed to some extent in books of this sort unless the editor is both fortunate in his selection of authors and extremely firm in his editing policy. The title of the book would imply that it it is intended to be a text devoted to that area of analytical chemistry dealing with the measurement of steroid hormones. Such books are usually written when a field of study has been sufficiently developed to allow the authors to present reasonably conscise and definite recommendations for the guidance of those who want to employ the techniques which have been developed. The present book is, in fact, a collection of reviews which might more reasonably have been called "Recent Advances in Steroid Hormone Analysis," to indicate that it is addressed more to experts interested in the development of these techniques, than to those who wish to use them. Even then, however, one is left wondering whether the material in this book should not have been published in existing journals devoted to reivews of this sort. This would have led to some very desirable pruning, and perhaps to the rejection of some of it. It remains to be noted that the printing and lay-out are excellent.

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The Structure and Function of Enzymes. By SIDNEY A. BERNHARD. W. A. Benjamin, Inc., New York, Amsterdam. 1968. xi + 324 pp. 21 × 13.8 cm. Paperback, $4.95. Cloth, $10.00.

Neither the undergraduate curriculum in chemistry nor biology in American universities provides enough time or background