| | | | | | —————————————————————————————————————— | | Found, % | | | |
|------------------|--|---|---|--|--|---|---|---|---|---|
| Z | ${f R}$ | \mathbf{R}_1 | \mathbb{R}_2 | Mp, °C | C | H | N | C | H | N |
| N | NHCOCH ₂ Cl | Н | H | 290 – 291 | 59.87 | 4.11 | 12.70 | 60.14 | 4.14 | 13.00 |
| \mathbf{N} | $\mathrm{NHCOCH_2CH_2Cl}$ | Н | H | 144 - 145 | 61.41 | 4.73 | 11.94 | 61.46 | 4.73 | 11.71 |
| \mathbf{N} | $ m NHCO(CH_2)_3Cl$ | Н | H^a | 114-115 | 62.74 | 5.27 | 11.27 | 62.78 | 5.39 | 11.16 |
| N | H | $NHCOCH_2Cl$ | H | 280 – 282 | 59.87 | 4.11 | 12.70 | 60.04 | 4.14 | 12.68 |
| \mathbf{z} | H | NHCOCH ₂ CH ₂ Cl | H | 134 - 135 | 61.41 | 4.73 | 11.94 | 61.60 | 4.84 | 12.24 |
| N | H | $\mathrm{NHCO}(\mathrm{CH_2})_3\mathrm{Cl}$ | Н | 122 - 123 | 62.74 | 5.27 | 11.27 | 62.70 | 5.55 | 11.10 |
| N | $NHCOCH_2Cl$ | H | $\mathrm{CH}_3{}^h$ | 162 - 165 | 61.41 | 4.73 | 11.94 | 60.90 | 4.65 | 11.68 |
| N | $NHCOCH_2CH_2Cl$ | H | CH_3 | 145 - 146 | 62.74 | 5.27 | 11.27 | 62.48 | 5.05 | 11.02^c |
| \mathbf{N} | $ m NHCO(CH_2)_3Cl$ | H | $\mathrm{CH_3}$ | 143 - 144 | 64.00 | 5.75 | 10.66 | 63.69 | 5.90 | 10.45 |
| CH | NHCOCH ₂ CH ₂ Cl | Н | H^d | 139-140 | 61.41 | 4.73 | 11.94 | 61.44 | 4.96 | 11.92 |
| $_{\mathrm{CH}}$ | $ m NHCO(CH_2)_3Cl$ | Н | H^d | 115-118 | 62.74 | 5.27 | 11.27 | 62.73 | 5.20 | 11.29 |
| $_{\mathrm{CH}}$ | $ m NHCO(CH_2)_4Cl$ | Н | Н | 139-141 | 64.00 | 5.75 | 10.66 | 63.81 | 5.60 | 10.66 |
| | N N N N N N CH CH | N NHCOCH₂Cl N NHCOCH₂Cl N NHCO(CH₂)₃Cl N H N H N H N H N H N HCOCH₂Cl N NHCOCH₂Cl N NHCOCH₂Cl CH NHCOCH₂Cl CH NHCOCH₂Cl CH NHCOCH₂Cl CH NHCOCH₂Cl | N NHCOCH₂CI H N NHCOCH₂CH₂CI H N NHCO(CH₂)₃CI H N H NHCOCH₂CI N H NHCOCH₂CH₂CI N H NHCO(CH₂)₃CI N NHCOCH₂CH₂CI H N NHCO(CH₂)₃CI H CH NHCOCH₂CH₂CI H CH NHCO(CH₂)₃CI H | N NHCOCH₂Cl H H N NHCOCH₂CH₂Cl H H N NHCO(CH₂)₃Cl H H N H NHCOCH₂Cl H N H NHCOCH₂Cl H N NHCOCH₂Cl H CH₃ ^b N NHCOCH₂Cl H CH₃ N NHCOCH₂Cl₂Cl H CH₃ N NHCOCH₂CH₂Cl H CH₃ CH NHCOCH₂CH₂Cl H H CH NHCO(CH₂)₃Cl H H | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ |

^a Gave 5-aminoisoquinoline on reaction with HN(CH₂CH₂OH)₂. ^b Gave 3-methyl-5-aminoisoquinoline on reaction with HN(CH₂-CH₂OH)₂. ^c Anal. Calcd: Cl, 14.26. Found: Cl, 14.20. ^d Gave 5-aminoquinoline on reaction with HN(CH₂CH₂OH)₂.

 ω -chloroacyl chlorides with the appropriate aminoheterocycle. It was hoped to convert these to alkylating agents similar to those prepared by Elderfield and LeVon³ from 8-aminoquinolines but in several preliminary experiments these amides were readily hydrolyzed in reactions with N,N-bis((2-hydroxyethyl)amine and the route was abandoned.

Experimental Section⁴

Preparation of Amides.—The appropriate aminoquinoline or aminoisoquinoline was treated with the appropriate ω -chloroacyl

chloride under the conditions of Elderfield and LeVon,³ the conditions of DiGangi,⁵ or more conveniently in CH₂Cl₂ or CHCl₃ to give after neutralization the amides listed in Table I.

p-N,N-Bis(2-chloroethyl)aminobenzoyl Derivative of 5-Aminoquinoline.—Use of p-[N,N-bis(2-chloroethyl)amino]benzoyl chloride and 5-aminoquinoline in the above sequence gave a 53% yield of solid, mp 169–172°. This compound exhibited no antineoplastic activity against Walker carcinosarcoma 256 at 25 mg/kg.

Anal. Calcd for $C_{20}H_{19}Cl_2N_3O$: C, 61.86; H, 4.93; N, 10.82; Cl, 18.26. Found: C, 61.82; H, 5.00; N, 10.82; Cl, 18.21.

Book Reviews

The Epidemiology of Tropical Diseases. By Oscar Felsenfeld. Charles C Thomas, Publisher, Springfield, Ill. 1966. xiv + 488 pp. 16.5×24 cm. \$14.75.

Only an insignificant number of American medicinal scientists and physicians are working in the field of tropical diseases, in spite of the fact that almost 500,000 Americans have been sent into jungles where they lie in foxholes, wade through vector-infested streams, and eat food that would be condemned as unsanitary in their home land. The reason for this apparent lack of interest is, quite simply, money. The U.S. Public Health Service must marshall its funds wisely for the health of the nation, and in the now increasingly rare intervals of "peace," tropical diseases present no major health hazard to most Americans. Most of the pharmaceutical industry sees little financial incentive in producing drugs that the impoverished underdeveloped countries in tropical regions could ill afford. This is a deplorable state of affairs both from a human and scientific point of view. Disregarding our inherent humanitarian impulses to help our fellow men to rid themselves of disease, we appear to be condemned by circumstances and by unwise policies to send wave after wave of our best young males to fight in tropical countries for many years to come. This alone should call for a major public and private effort to sponsor research in tropical diseases. Scientifically, huge unexplored areas here the medicinal and medical investigator to apply to them experiments in fundamental science and clinical art.

The textbook by Felsenfeld makes a valuable contribution to this neglected field and should be required reading for any committee that toys with plans for research on tropical maladies. It can be read profitably by epidemiologists and by laymen. The infectious process, including routes and vectors of infections, start off the book and lead next to control measures by sanitation and immunization. The next four major sections are devoted to detailed discussions of the epidemiology of bacterial, mycotic, parasitic, rickettsial, and viral diseases encountered in hot, humid belts; some of these infections overlap with conditions prevalent in North America as well. The final section of the book deals with noncommunicable diseases of nutritional and occupational origin, malignancies, dental and cardiovascular disorders, and addiction and mental diseases. Here again the tropics hold no privileged position, and much of what the author has observed there would apply to domestic conditions.

The book is clearly written, well printed, and thoroughly readable. There is an adequate subject index, and at the end of each section a list of references to books, recent monographs, and reviews.

University of Virginia Charlottesville, Virginia Alfred Burger

Developmental and Metabolic Control Mechanisms and Neoplasia. A Collection of Papers Presented at the Nineteenth Annual Symposium on Fundamental Cancer Research, 1965, at The University of Texas M. D. Anderson Hospital and Tumor Institute. The Williams and Wilkins Company, Baltimore, Md. 1965. x + 514 pp. 16×23.7 cm. \$16.00.

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⁽³⁾ R. C. Elderfield and E. F. LeVon, J. Org. Chem., 25, 1576 (1960).

⁽⁴⁾ Analyses by Spang Microanalytical Laboratory, Ann Arbor, Mich. Melting points are taken in capillaries and are corrected.

⁽⁵⁾ F. E. DiGangi, J. Am. Pharm. Assoc., 44, 136 (1955).