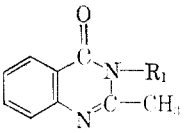
TABLE I
2-METHYL-3-R_1-4-QUINAZOLONE



R_1	M.p., °C.	Yield, %	Formula	Calcd., % C	H	N	Found, % C	H	N
2-Pyridyl	164–165	65	$C_{14}H_{11}N_3O$	70.8	4.62	17.7	70.44	5.1	17.1
3-Pyridyl[a]	225–226	68	$C_{14}H_{11}N_3O \cdot HCl$	61.42	4.31	15.35	60.83	4.81	15.05
4-Pyridyl	144–146	58	$C_{14}H_{11}N_3O$	70.8	4.62	17.7	69.83	5.7	17.2
2-Pyridylmethyl	122	57	$C_{15}H_{13}N_3O$	71.7	5.1	16.7	71.87	5.5	16.0
3-Pyridylmethyl	116	49	$C_{15}H_{13}N_3O$	71.7	5.1	16.7	71.21	5.64	16.1
4-Pyridylmethyl	127	54	$C_{15}H_{13}N_3O$	71.7	5.1	16.7	71.28	5.47	16.4
5-Quinolyl	208–209	56	$C_{18}H_{13}N_3O$	75.26	4.53	14.63	74.92	4.71	15.06

[a] The free base could not be crystallized and hence was reported as hydrochloride of 2-methyl-3-pyridyl-4-quinazolone.

et al.,[5] have reported that inhibitors of monoamine oxidase possess pronounced anticonvulsant properties. 4-Aminoquinoline has been shown to be a potent inhibitor of this enzyme, as compared to 4-aminopyridine which was almost devoid of such inhibitory activity.[6] On the basis of these observations we have synthesized 2,3-disubstituted quinazolones from aminopyridines and 5-aminoquinoline following the method of Bogert, *et al.*[7]

Experimental[8]

Molar proportions of acetanthranil (m.p. 78–80°) and the appropriate amines were mixed together in a round-bottomed flask. The contents of the flask were first heated on a low flame and then on a full flame. On cooling, the jelly-like mass which separated out crystallized yielding 2,3-disubstituted quinazolones in good yield.

The various pyridine derivatives used were 2-amino-, 3-amino-, and 4-aminopyridines, and 2-aminomethyl-, 3-aminomethyl-, and 4-aminomethylpyridines. In addition, 5-aminoquinoline was also used for the preparation of a quinazolone. All quinazolones were crystallized from a mixture of ethyl alcohol and ether (1:1) except the one formed from 4-aminopyridine which was crystallized with methyl alcohol only. The characterization of these 2,3-disubstituted quinazolones was done by their sharp melting points and also by analysis. The results are summarized in Table I.

(5) J. P. Darwin, A. Shore, and B. B. Brodie, *Proc. N. Y. Acad. Sci.*, **80**, 643 (1959).

(6) P. N. Kaul, *J. Pharm. Pharmacol.*, **14**, 243 (1962).

(7) T. A. Williamson, "Heterocyclic Compounds," Vol. 6, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1957, p. 334.

(8) Melting points were taken in a capillary tube and are uncorrected.

9-Thienylanthracenes[1]

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The title compounds were prepared as part of an air pollution study program to make new polycyclic aromatic compounds available for carcinogenicity testing. The synthetic routes to these compounds involve extensions to useful reactions previously recorded.[4]

(1) This investigation was supported by research Grant AP-00088-06 from the Division of Air Pollution, Bureau of State Services, Public Health Service.

(2) Taken from the Doctorate theses of S. G. Quo and P. Polss presented to the Virginia Polytechnic Institute in 1959 and 1962, respectively.

(3) N. D. E. A. Fellow 1960–1963, Eastman Kodak Fellow 1963–1964.

(4) F. A. Vingiello, S. G. Quo, and J. Sheridan, *J. Org. Chem.*, **26**, 2669 (1961).

Experimental[5,6]

2-(2-Thenoyl)diphenylmethane. A.—A Grignard reagent was prepared from 7.2 g. (0.30 g.-atom) of magnesium and a solution of 50 g. (0.30 mole, 30 ml.) of 2-bromothiophene in anhydrous ether. After completion of reaction, most of the ether was distilled while 47 g. (0.24 mole) of 2-cyanodiphenylmethane dissolved in anhydrous benzene was added. The mixture was heated under reflux for 18 hr. and worked-up in the usual way. The product was a viscous oil, b.p. 192–195° (0.5 mm.), 59 g. (88%). It was crystallized from ethanol, m.p. 43–44°.

Anal. Calcd. for $C_{18}H_{14}OS$: C, 77.66; H, 5.07; S, 11.52. Found: C, 77.53; H, 4.97; S, 11.52.

The product was oxidized quantitatively using sodium dichromate in glacial acetic acid to give 2-(2-thenoyl)benzophenone, m.p. 135–136° (from ethanol).

Anal. Calcd. for $C_{18}H_{12}O_2S$: C, 73.94; H, 4.14. Found: C, 73.69; H, 4.24.

B.—A Grignard reagent was prepared from 37 g. (0.15 mole of 2-bromodiphenylmethane and 3.9 g. (0.16 g.-atom) of magnesium in dry ether. After most of the magnesium had reacted, the ethereal solution of the Grignard reagent was transferred, under nitrogen, to a separatory funnel and added slowly to a boiling solution of 22 g. (0.15 mole) of 2-thenoyl chloride in dry benzene. Solvent was removed until the boiling temperature was 66°, and the mixture was heated for 4.5 hr., then decomposed and worked-up to give 16 g. (38%) of product, identical with that obtained by A.

2-(3-Thenoyl)diphenylmethane. A.—This compound could not be prepared as was the 2-isomer, but resort had to be had in the entrainment method using ethyl bromide. The product, b.p. 180–185° (0.5 mm.), was a viscous oil obtained in 58% yield.

Anal. Calcd. for $C_{18}H_{14}OS$: C, 77.66; H, 5.07; S, 11.52. Found: C, 77.64; H, 5.09; S, 11.24.

B.—The compound was prepared essentially as was the 2-isomer. The product, b.p. 127° (0.20 mm.) (spinning band column), was a viscous oil obtained in yield 37%.

9-(2-Thienyl)anthracene.—A mixture of 34 g. (0.122 mole) of 2-(2-thenoyl)diphenylmethane, 1200 ml. of glacial acetic acid, and 600 ml. of 48% hydrobromic acid was heated under reflux for 44 hr. The solution was cooled, diluted with water, and refrigerated overnight giving 20 g. (65%) of crystals, m.p. 113–114°. Recrystallization from absolute ethanol gave an analytical sample as yellow needles, m.p. 113.5–114.0°, which fluoresced green under ultraviolet light.

Anal. Calcd. for $C_{18}H_{12}S$: C, 83.03; H, 4.65; S, 12.32. Found: C, 82.81; H, 4.97; S, 12.18.

The same product was obtained using phosphorus pentoxide or hydrogen phenyl phosphate as the acid catalyst.

The product formed a deep violet 1:2 adduct with 2,4,7-trinitrofluorenone, m.p. 166–167°.

Anal. Calcd. for $C_{44}H_{22}N_6O_{14}S$: C, 59.33; H, 2.49; N, 9.43; S, 3.60. Found*: C, 59.27; H, 2.41; N, 9.44; S, 3.67.

(5) Analyses by Geller Laboratories, Bardonia, N. Y., except those marked with an asterisk which were performed by Galbraith Laboratories, Knoxville, Tenn.

(6) Melting points are corrected, boiling points are not.

9-(3-Thienyl)anthracene.—This compound was obtained essentially as was the '2-isomer' above in 80% yield from the corresponding ketone using hydrobromic acid as the catalyst. Recrystallization from absolute ethanol gave an analytical sample as yellow needles, m.p. 122.0–122.5°, which fluoresced green under ultraviolet light.

Anal. Calcd. for $C_{18}H_{12}S$: C, 83.03; H, 4.65; S, 12.32. Found: C, 83.10; H, 4.76; S, 12.06.

The black 1:2 adduct with 2,4,7-trinitrofluorenone melted at 167–168°.

Anal. Calcd. for $C_{44}H_{22}N_6O_{14}S$: C, 59.33; H, 2.49; N, 9.43; S, 3.60. Found*: C, 59.44; H, 2.53; N, 9.38; S, 3.37.

Book Reviews

The Neomycins and Related Antibiotics. By KENNETH L. RINEHART, JR. John Wiley and Sons, Inc., New York, N. Y. 1964. 136 pp. 12 × 18 cm.

The antibiotic neomycin was discovered in 1949 and the fact that its gross architecture and stereochemistry were not completed until 1962 attests to the degree of difficulty this type of problem presents. The chemical and medical literature has desperately needed clarification in the neomycin field due to the large number of similar and identical antibiotics which have been reported throughout the world. To this end Professor Rinehart has done an excellent job and yeoman service in identifying and correlating these substances. It was fortunate perhaps that two closely related antibiotics, kanamycin and paromomycin, appeared on the clinical horizon in the late fifties since techniques used in the degradative procedures of one aided progress in the others.

The book offers many interesting examples in the application of periodate oxidation, Hudson's rotational rules, and nuclear magnetic resonance to the elucidation of oligosaccharide structures. In some instances, however, structures have been postulated by presumptive rather than conclusive evidence but are interesting nonetheless in that they offer the reader a mental exercise in sugar conformational analysis. Of particular interest is the novel use of cuprammonium rotation data to the determination of absolute configuration of monosubstituted deoxystreptamines. A welcome addition to the chemical studies is a chapter on biosynthetic considerations. Although incomplete, it should offer the microbiologist valuable information relative to antibiotic precursor studies.

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Experimental Chemotherapy. Volume II. Chemotherapy of Bacterial Infections. Part I. Edited by R. J. SCHNITZER and F. HAWKING. Academic Press Inc., New York, N. Y. 1964. xvii + 614 pp. 16 × 23 cm. $23.00. [For a review of Vol. I, see *J. Med. Chem.*, **6**, 825 (1963)].

In almost all fields of chemotherapy the triumphs of the late 1940's and the early 1950's have been dampened by the emergence of drug-resistant organisms, and the flare-up of nearly forgotten infections in less treatable, or even untreatable, forms. Moreover, systemic antibacterial therapy is mostly bacteriostatic rather than bactericidal, and as G. P. and A. S. Youmans put it in the present volume (p. 394), "there is, therefore, a real need for new and more eradicative drugs." This should not detract from the magnificent achievements of the antibiotics and the synthetic antibacterial agents which have contributed so much to increased longevity and healthier living. Nevertheless, the appearance of a new treatise on all aspects of bacterial chemotherapy is a timely event and should guide the investigator to future needs of researches in this field.

The antibacterial dyestuffs, with emphasis on acridine derivatives, are reviewed by C. H. Browning. This section is the only connection to the early history of antibacterial agents in this book. It is to be regretted that space did not permit the inclusion of many other older antibacterial agents which were tried and discarded before the advent of decisively active drugs for a given infection. Many valuable "leads" are stacked away among those forgotten compounds. In a time when radical departures from useful drugs are being sought to overcome problems of bacterial resistance and persistence, some of those old studies may well have been unearthed again.

H. J. Rogers considers the structure and functions of bacteria *vs.* mammalian cells, and derives from these facts theories of action of the sulfonamides and antibiotics which affect the synthesis of the bacterial cell wall. In a well-written chapter, R. Knox discusses theoretical aspects of the strategy and tactics of antibacterial chemotherapy, from serendipity through *in vitro* to *in vivo* requirements. D. J. Kushner writes about the resistance of bacteria to harsh and destructive environmental conditions such as heat, chemical concentrations, radiation, pH, heavy metals, enzyme inhibitors, surfactants, and disinfectants Special topics include the chemotherapy with sulfonamides (L. Neipp) and the pharmacology of these drugs (R. E. Bagdon) the nitrofurans (H. E. and M. F. Paul), topical antibacterial, (R. J. Schnitzer), and therapeutic agents for tuberculosis (G. Ps and A. S. Youmans) and leprosy (P. C. Eisman). These special. chapters are searching and critical evaluations of available. methodology and the meaning of the procedures, and should satisfy the demanding reader as well as those who look for overall information on one of these subjects.

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Metabolic Inhibitors—A Comprehenisive Treatise. Volume II. Edited by R. M. HOCHSTER and J. H. QUASTEL. Academic Press Inc., New York, N. Y. 1964. xvii + 753 pp. 15 × 21.5 cm. $29.00.

We know that the multitude of natural metabolites in a given "living" system balance each other to produce the "normal" condition of the system. A deletion of one or several metabolites upsets this balance. This situation may remedy itself by the establishment of a new balance in which an induced overproduction of a previously less active metabolite makes up for the deletion of the lost vital factors. Or else, an extraneous chemical, a drug, or an internal chemical arising through an induced physical change of the biochemical environment may restore the upset balance, occasionally upsetting another facet in an undesired side effect. Whatever we insert into a biological system, be it a nutrient or a corrective medicinal agent, will preoccupy enzymes, tie up other natural chemicals, or cause them to react chemically, and thereby temporarily or permanently remove them from the integrated biochemical scene. All these substances are metabolic antagonists. They range from the irreversible inhibitors to the kinetically most unstable antimetabolite systems; they interfere with the biosynthesis of needed metabolites, or compete with the finished product for a reactive site of a macromolecular biocatalyst.

The present volume, the second and the last one in this series, attempts to cover the kaleidoscopic variety of all grades of antimetabolites which have not been discussed in Volume I [see *J. Med. Chem.*, **6**, 828 (1963)]. Expert authors have been chosen for each chapter, and each appears to have done his level best to survey critically, broadly, and with restraint his assigned field about which he knows so much. The editors must have had a hard task coordinating these interwoven and overlapping chapters. Just as even an experienced biochemist will be troubled by the relative lack of specificity of the vast majority of antimetabolites, thus the editors must have suffered from the overlapping of chapters. However, this could have been corrected had the editorial work been done more carefully. To take a specific point, the well-presented chapter on mono- and polyamine analogs by E. A. Zeller is followed by a survey of inhibitors of catecholamine metabolism (T. L. Sourkes and A. D'Iorio) which