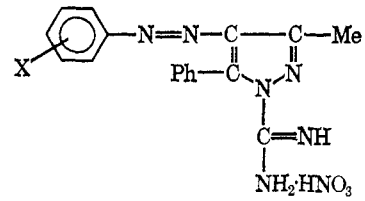
TABLE I

CHARACTERISTICS OF 4-ARYLAZO-1-(GUANYL NITRATE)-3-METHYL-5-PHENYLPYRAZOLES



No.	X	Yield, %	Mp, °C	Color[a]	Formula	Analyses
1	3-Cl	65	144	DON	$C_{17}H_{16}ClN_7O_3$	Cl, N
2	4-Cl	63	171	ON	$C_{17}H_{16}ClN_7O_3$	C, H, Cl, N
3	2-Me	67	178	BN	$C_{18}H_{19}N_7O_3$	C, H, N
4	3-Me	70	158	BN	$C_{18}H_{19}N_7O_3$	C, H, N
5	2-NO_2	70	139	ON	$C_{17}H_{16}N_8O_5$	C, H, N
6	3-NO_2	68	142	YN	$C_{17}H_{16}N_8O_5$	C, H, N
7	2-Br	72	148	OP	$C_{17}H_{16}BrN_7O_3$	Br, N
8	4-Br	70	176	ON	$C_{17}H_{16}BrN_7O_3$	C, H, N, Br
9	2-MeO	65	140	OYP	$C_{18}H_{19}N_7O_4$	C, H, N
10	2-EtO	70	163	YN	$C_{19}H_{21}N_7O_4$	C, H, N
11	4-EtO	72	160	ON	$C_{19}H_{21}N_7O_4$	C, H, N
12	4-SO_2NH_2	70	187	LtYN	$C_{17}H_{18}N_8O_5S$	C, H, S
13	2,3-Me_2	65	143	YP	$C_{19}H_{21}N_7O_3$	C, H, N
14	2,5-$(MeO)_2$	68	165	DYN	$C_{19}H_{21}N_7O_5$	C, H, N
15	2,4-$(MeO)_2$	70	174	OYN	$C_{19}H_{21}N_7O_5$	C, H, N
16	2,5-$(EtO)_2$	70	156	BP	$C_{21}H_{25}N_7O_5$	C, H, N
17	2,4-Cl_2	65	240	LtBP	$C_{17}H_{15}Cl_2N_7O_3$	C, H, Cl
18	2,4-Br_2	68	171	YON	$C_{17}H_{15}Br_2N_7O_3$	C, H, Br
19	2,5-Br_2	65	259	YON	$C_{17}H_{15}Br_2N_7O_3$	Br, N
20	2-Cl-6-Me	60	181	ON	$C_{18}H_{18}ClN_7O_3$	C, H, Cl

[a] B, brown; D, dark; Lt, light; N, needles; O, orange; P, plates; Y, yellow.

Antiviral Activity.—Ib [X = 3-Cl, 2,4-$(NO_2)_2$] and IIb [X = 2-Cl, 2-NO_2, 4-NO_2, and 4-SO_2NH_2] were screened for antiviral activity against Rhino virus 1059 and 33342 and Respiratory Syncytical Long. There was no plaque inhibition.

Anti-*Trichinella spiralis* Activity.—Tests on Ib [X = 4-Cl, 3-NO_2, 4-NO_2, 4-SO_2NH_2, and 2,5-Cl_2] and IIa [X= 4-Cl, 3-Cl, 4-NO_2, 3-NO_2, 2-NO_2, 4-SO_2NH_2, 2-Cl-4-NO_2, and 2,5-Cl_2] by oral administration to chicks at 0.05% of diet infected with *Eimeria tennela* showed essentially no activity.

Experimental Section

Melting points were taken with a Kofler hot-stage type apparatus and are uncorrected. 2-Arylhydrazono-1-phenylbutane-1,2,3-triones were prepd by the method of Garg, *et al.*[4]

4-(4-Chlorophenylazo)-1-(guanyl nitrate)-3-methyl-5-phenylpyrazole.—Equimolar quantities of aminoguanidine nitrate and 2-(4-chlorophenylhydrazono)-1-phenylbutane-1,2,3-trione (0.005 mole) were dissolved in hot EtOH (30 ml) and refluxed for 1 hr. To this was added 30% HNO_3 until the pH of the reaction mixt became 1. It was again refluxed for 4.5 hr. On cooling, shining crystals sepd out. The characteristics of the 4-arylazo-1-guanylnitrate-3-methyl-5-phenylpyrazoles prepd by similar methods are given in Table I.

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2,5-Dimethoxy-4-methylphenylalanine

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Interest in the mode of action of centrally active phenethylamines, particularly the amphetamines,[1] prompts us to report the synthesis of the title compound (I), which was prepared during the course of other work. I is a possible amino acid precursor of the corresponding phenethylamine, which is 5 times as potent as mescaline.[2] The classical azlactone synthesis[3] of amino acids was unsuccessful because the benzaloxazolone could not be reduced either catalytically or with NaHg, but I was readily obtained from 2,5-dimethoxy-4-methylbenzyl chloride[4] by acetamidomalonate condensation and acidic hydrolysis.

(1) A. T. Shulgin, T. Sargent, and C. Naranjo, *Nature (London)*, **221**, 538 (1969); R. M. Pinder, R. W. Brimblecombe, and D. M. Green, *J. Med. Chem.*, **12**, 322 (1969); B. T. Ho, W. M. McIsaac, R. An, L. W. Tansey, K. E. Walker, L. F. Englert, and M. B. Noel, *ibid.*, **13**, 26 (1970).

(2) B. T. Ho, L. W. Tansey, R. L. Balster, R. An, W. M. McIsaac, and R. T. Harris, *ibid.*, **13**, 134 (1970).

(3) H. E. Carter, *Org. React.*, **3**, 198 (1946).

(4) T. H. Posternak, R. Huguenin, and W. Alcalay, *Helv. Chim. Acta*, **39**, 1564 (1956); in our hands, this method gave considerably more 2,2′,5,5′-tetramethoxy-4,4′-dimethyldiphenylmethane than is reported. The desired benzyl chloride is obtd better by LAH reduction of 2,5-dimethoxy-4-methylbenzaldehyde[5] followed by chlorination with $SOCl_2$–C_6H_6.

(5) A. A. R. Sayigh, H. Ulrich, and M. Green, *J. Chem. Soc.*, 3482 (1964); UpJohn Co., French Patent 1,415,670, 1965; *Chem. Abstr.*, **64**, 5002 (1966).

Experimental Section[6]

2-Phenyl-4-(2,5-dimethoxy-4-methylbenzal)-5-oxazolone.—A mixt of hippuric acid (3.6 g, 0.02 mole), 2,5-dimethoxy-4-methylbenzaldehyde[5] (3.6 g, 0.02 mole), NaOAc (1.6 g, 0.02 mole), and Ac_2O (6.1 g, 0.06 mole) was refluxed for 2 hr. H_2O (50 ml) was added to the cooled mixt, and the solid was filtered off and recrystd from EtOH, yield 4.5 g (69%), mp 215–216°. *Anal.* ($C_{19}H_{17}NO_4$) C, H, N.

Diethyl α-Acetamido-α-(2,5-dimethoxy-4-methylbenzyl)-malonate (II).—A mixt of solns of 2,5-dimethoxy-4-methylbenzyl chloride[4] (20 g, 0.1 mole) and diethyl acetamidomalonate (21.7 g, 0.1 mole) in EtOH (100 ml) was added over 15 min to a soln of Na (2.3 g, 0.1 g-atom) in EtOH (60 ml), and the soln was refluxed for 2 hr. EtOH was removed on the rotary evaporator, H_2O (100 ml) was added to the residue, and the cryst solid was filtered off and dried. Recrystn from petr ether (bp 100–120°) gave 23 g (61%) of colorless needles, mp 131–132°. *Anal.* ($C_{19}H_{27}NO_7$) C, H, N.

2,5-Dimethoxy-4-methylphenylalanine·HCl (I).—II (7.6 g, 0.02 mole) was refluxed for 5 hr with 100 ml of 5 *N* HCl. The resulting brown soln was cooled to 0°, and the solid was filtered off and recrystd from EtOH–petr ether (bp 60–80°), yield 3.6 g (67%), mp 251–253°. *Anal.* ($C_{12}H_{17}NO_4 \cdot HCl$) C, H, N.

Ethyl 2,5-Dimethoxy-4-methylphenylalaninate·HCl, prepd by esterification of I with ethanolic HCl, had mp 165–166° (EtOH–Et_2O). *Anal.* ($C_{14}H_{21}NO_4 \cdot HCl$) C, H, N.

(6) Melting points are uncorrected. Anal. were within ±0.4% of theor values. Satisfactory ir, uv, and nmr spectra were obtd for all compds.

Book Reviews

Role of Cyclic AMP in Cell Function. Advances in Biochemical Pharmacology. Volume 3. Edited by P. Greengard and E. Costa. Raven Press, New York, N. Y. 1970. 386 pp. 24.2 × 16 5 cm. $15.95.

Since the announcement of the discovey of cyclic AMP as the intracellular mediator of the glycogenolytic effect of epinephrine and glucagon by Earl W. Sutherland in 1960, a vast body of findings concerning the role of cyclic AMP in neuronal functions and in many organ systems has accumulated. The decisive factor most widely studied has been the adenyl cyclase system which catalyzes the conversion of ATP to cyclic AMP and inorganic pyrophosphate. The present volume represents the proceedings of a conference held in February 1970 in which the background for the role of cyclic AMP in the function of the neuron was discussed in all its ramifications. While concentrating on brain, central synapses, the pineal gland, and other CNS tissues, neuromuscular and other peripheral locations have not been neglected. On the enzyme level, the interplay between phosphodiesterases, adenyl cyclase, lipases, and *N*-acetyltransferase are surveyed. The actions of several hormones (norepinephrine-types, prostaglandins, glucagon, and polypeptide hormones) are the subject of several chapters. Biochemists, neuropharmacologists, and physiologists will find a wealth of reference material in this book, and stimulating suggestions for further work in a field of overriding fundamental importance.

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Biochemistry of Simple Neuronal Models. Advances in Biochemical Psychopharmacology. Volume 2. Edited by E. Costa and E. Giacobini, with 22 contributors. Raven Press, New York, N. Y. 1970. 382 pp. 16.5 × 24 cm. $15.95

This symposium (Milan, 1969) volume starts with a quotation from a paper by Sir John Eccles: "...neurochemistry provides the key to some of the most perplexing problems of brain science,....how the brain is put together, and also the chemical specificity involved in its normal activities. The day-to-day metabolism, all the membrane phenomena, the pumping of ions, and the sensing and recognition of cell surfaces all need study. How does a nerve fiber grow to make a distant connection with the right nerve cell....?" These thoughts set the stage for the questions discussed in this book, among them: biochemistry of synaptic plasticity in single neurons; axonal transport of amine storage granules; a contractile model of the release of transmitters from storage; neuronal uptake processes; the GABA system; ACh metabolism at vertebrate neuromuscular junctions; a biophysical model for storage and release to monoamines; neuromembrane electrogenesis; membrane protein synthesizing machinery of the axon; do specific biochemical correlates to learning processes exist in brain cells?

These questions with some free discussions from the conference floor, may give an idea of the scope of the book. In an area as new, and as active as the biochemistry of neuronal structures and functions, one cannot help but feel that multiple explanations of the multitude of observations are unavoidable. However, the time may come when unitarian concepts may emerge. This volume is an attempt to lead our thinking in this direction.

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Survey of Organic Syntheses. By Calvin A. Buehler and Donald E. Pearson. Wiley-Interscience, New York, N.Y. ix + 1166 pp. 16 × 24 cm. $27.50.

This book consists of 20 chapters each of which discusses a number of methods for synthesis of a given functional group, typical chapter titles being: alkanes, cycloalkanes, and arenes; halides; acyl halides; nitro compounds. Each chapter then lists methods for synthesis of the function group from various types of starting materials, *e.g.*, for phenols: from phenylhydroxylamines; from cyclodienones; from cyclic glycols. Each reaction type is subsequently illustrated by a succinct experimental description of 1 or 2 specific examples and then by a larger number of examples for which yield data, starting material, and literature reference are given. The total number of literature references cited is very impressive, at least several thousand.

This work is similar in some ways to both Wagner and Zook, "Synthetic Organic Chemistry," and W. Theilheimer, "Synthetic Methods of Organic Chemistry." It will certainly serve to update Wagner and Zook although unlike Wagner and Zook there is no tabular display of synthetic data. This single volume of course provides less extensive coverage than Theilheimer but it gives a brief discussion on the scope and mechanism of many of the reaction types considered, information which is not present in Theilheimer.

The selection of reactions seems to strike a reasonable balance between rather standard reaction types and more recent synthetic development and also includes examples of numerous reactions described in the literature in the 1950's which would appear to have unrealized potential.

I do not feel the book would lend itself to use as an advanced text. The brevity of the mechanistic discussion permits only the most general type of discussion and the language is occasionally imprecise. It should, however, see wide use as a first source of information for chemists faced with a synthetic problem which is amenable to a functional group approach and would be an excellent book for one interested in broadening his background of synthetically useful reactions.

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