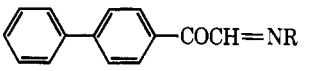
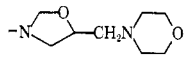
TABLE I

HYDRAZINE DERIVATIVES OF (4-BIPHENYLYL)GLYOXAL



Compd	R	Mp, °C	Formula	C, % Calcd	C, % Found	H, % Calcd	H, % Found	N, % Calcd	N, % Found	Equiv wt Calcd	Equiv wt Found
I	$-N(CONH_2)CH_2CO_2H$	205–206[a]	$C_{17}H_{15}N_3O_4$	62.8	62.7	4.65	4.77	...	...	325	322
II		178–180[a]	$C_{22}H_{23}N_3O_4$	67.2	67.0	5.89	6.03	...	...	393	396
III		277[a]	$C_{17}H_{13}N_3O_3$	66.4	66.6	4.26	4.15	...	...	301	304
IV	$-NHCH_2CH_2OH$	120–122	$C_{16}H_{16}N_2O_2$	71.6	71.6	6.03	6.14	10.4	10.4	...	...
V	$-NHCH_2CO_2C_2H_5$	96–98[b]	$C_{18}H_{18}N_2O_3$	70.3	70.0	6.22	5.95	8.6	8.9	...	...
VI	$-NHCH_3$	107–108[c]	$C_{15}H_{14}N_2O$	75.6	75.7	5.92	5.81	11.8	11.9	...	...
VII	$-N(CH_3)_2$	114–115	$C_{16}H_{16}N_2O$	76.2	76.2	6.34	6.20	11.1	11.2	...	...

[a] Recrystallized from EtOH. [b] From benzene. [c] From petroleum ether (60–80°).

Experimental Section[4]

Intermediate Hydrazines.—Semicarbazidoacetic acid,[5] 3-amino-5-morpholinomethyl-2-oxozalidine (prepared *in situ* from the benzylidene derivative[6]), 1-aminohydantoin,[7] and ethyl hydrazinoacetate[8] were made by procedures based on literature preparations. The remaining hydrazines were obtained from commercial sources.

Preparation of Hydrazones.—The hydrazones listed in Table I were prepared from 4-biphenylylglyoxal hydrate and the hydrazine in a solvent such as ethanol or aqueous ethanol, and the method is typified by the following example.

Ethyl (4-Biphenylylglyoxylidene)hydrazinoacetate (V).—To a stirred solution of 4-biphenylylglyoxal hydrate (18.3 g, 0.08 mole) in hot ethyl alcohol (100 ml) was added a solution of ethyl hydrazinoacetate hydrochloride (12.4 g, 0.08 mole) in hot water. The solution was adjusted to pH 6 by the addition of sodium acetate and stirring was continued until it had attained room temperature. The solid which separated on standing overnight was collected and recrystallized from benzene affording the pure hydrazone as slender needles, mp 96–98°, yield 12.1 g (49%).

Infrared Spectra.—The infrared spectra of the hydrazone derivatives I, II, III, and VII showed the expected aromatic carbonyl absorptions at 1650–1654 cm^{-1} but those of IV, V, and VI were anomalous and lacked the expected carbonyl or amino absorptions. The latter phenomenon is attributed to intramolecular hydrogen bonding involving the proton on the secondary nitrogen atom. Infrared spectra of V and VI in CCl_4 solution (1, 0.5, and 0.25%) lacked absorptions in the carbonyl region but peaks due to bonded hydroxyl or amino groups appeared at 3458, 3420, and 3210 cm^{-1}.

(4) Melting points were recorded using an Electrothermal melting point apparatus comprising a gas-heated block and a thermometer calibrated for exposed stem. Microanalyses are by Mr. M. Graham and spectra by Miss E. V. Eggington. The infrared spectra of all of the products were recorded with a Hilger H. 800 instrument.

(5) W. Traube and E. Hoffa, *Ber.*, **31**, 162 (1898).

(6) (a) D. L. Heywood and S. B. Phillips, *J. Am. Chem. Soc.*, **80**, 1257 (1958); (b) G. Gever, British Patent 843,834 (1957); *Chem. Abstr.*, **51**, 18007 (1957).

(7) D. Jack, *J. Pharm. Pharmacol.*, **11**, Suppl 108 T (1959).

(8) A. Darapsky and M. Prabhazar, *Ber.*, **45**, 1654 (1912).

Synthesis of 1-Benzyltryptamine

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1-Benzyltryptamine is related to a series of potent serotonin antagonists, *e.g.*, 1-benzyl-2-methyl-5-methoxytryptamine (BAS),[2] and has been prepared in 40–50% yield by the Fischer cyclization of 4-aminobutyraldehyde benzylphenylhydrazone.[3,4]

We have prepared 1-benzyltryptamine and the α-methyl homolog in comparable yields in a three-step synthesis as described in the Experimental Section.

Experimental Section[5]

The properties of I–VII are listed in Table I.

1-Benzyl-3-indolealdehyde (I).—A mixture of 145 g (1.0 mole) of 3-indolealdehyde,[6] 125 ml of benzyl chloride, 140 g of anhydrous K_2CO_3, and 300 ml of pure dimethylforamide (DMF) was vigorously stirred and heated for 2 hr, the cooled solution was poured into 2 l. of water, and the precipitated solid was collected, dried, and recrystallized.

1-Benzyl-3-(2-nitrovinyl)indole (II).—The aldehyde I (23.5 g, 0.1 mole) was heated for 30 min with 100 ml of nitromethane and 6 g of NH_4OAc. After cooling, the yellow precipitate was filtered off and washed with methanol.

1-Benzyltryptamine (III).—A solution of 27.8 g (0.1 mole) of II in 150 ml of tetrahydrofuran (THF) was added to 21.0 g of $LiAlH_4$ in 200 ml of THF. The mixture was stirred and refluxed for 1.5 hr, cooled, treated with THF–water (3:1) until evolution of hydrogen ceased, and filtered, the solvents were removed, and the residue was distilled under reduced pressure.

1-Benzyl-3-(2-methyl-2-nitrovinyl)indole (IV). A.—Compound I (94.0 g, 0.4 mole) heated with 100 ml of nitroethane and 20 g of NH_4OAc at 100° for 30 min gave a yellow product.

B.—3-(2-Methyl-2-nitrovinyl)indole[7] (20.2 g, 0.1 mole), 14 ml of benzyl chloride, 14.0 g of anhydrous K_2CO_3, and 150 ml of DMF were stirred and heated together at 110–120° for 3 hr. The mixture was poured into cold water and the solid precipitate was collected and recrystallized.

An attempt to obtain this compound from 3-(2-methyl-2-nitrovinyl)indole and benzoyl chloride in pyridine at room temperature was unsuccessful.

1-Benzyl-*dl*-α-methyltryptamine (V).—Compound IV (14.6 g 0.05 mole) was dissolved in 400 ml of ether–THF (1:1) and added to 8.5 g of $LiAlH_4$ in 200 ml of ether. The mixture was stirred for 2 hr, decomposed by adding 20 ml of ethyl acetate followed by 35 ml of 15% NaOH, and filtered off. The filtrate was concentrated, and the basic residue was distilled under reduced pressure.

1-Benzoyl-3-(2-methyl-2-nitrovinyl)indole (VI).—Benzoyl chloride (7 ml) was slowly added to 10.1 g (0.05 mole) of 3-(2-

(1) Visiting Scientist, Clinical Neuropharmacology Research Center, National Institute of Mental Health, 1961–1963, on leave from the Israel Institute for Biological Research, Ness Ziona, Israel.

(2) E. N. Shaw and D. W. Woolley, *J. Pharmacol. Exptl. Therap.*, **116**, 164 (1956).

(3) U. Hörlein, *Chem. Ber.*, **87**, 463 (1954).

(4) R. Duschinsky, U. S. Patent 2,642,438 (1953); *Chem. Abstr.*, **48**, 5230 (1954).

(5) Melting points were determined on a Fisher-Johns apparatus; boiling points are uncorrected.

(6) Ph. N. James and H. R. Snyder, "Organic Syntheses," Coll. Vol. IV John Wiley and Sons, Inc., New York, N. Y., 1963, p 539.

(7) E. H. P. Young, *J. Chem. Soc.*, 3493 (1958).

TABLE I

No.	Bp (mm) or mp, °C	Recrystn solvent	Yield, %	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
I	113–114	Ethanol	94	$C_{16}H_{13}NO$	81.68	5.57	5.95	81.60	5.54	5.72
I[a]	292 dec			$C_{22}H_{17}N_5O_4$	63.61	4.13	16.87	63.88	4.46	17.12
II	130.5–131.5	Methanol–ethyl	81	$C_{17}H_{14}N_2O_2$			10.07			9.92
III	198–200 (0.5)[b]	acetate	59	$C_{17}H_{18}N_2$			11.19			10.89
III[c]	152–153	Ethanol		$C_{23}H_{21}N_5O_7$	57.62	4.42	14.61	57.95	4.74	15.13
IV	117–118	Ethanol	87[d] 75[e]	$C_{18}H_{16}N_2O_2$	73.94	5.52	9.58	73.82	5.75	9.42
V	190–195 (0.1)		73	$C_{18}H_{28}N_2$	81.77	7.63	10.60	81.40	7.58	10.22
V[f]	193–194	Toluene–ethanol		$C_{18}H_{21}ClN_2$	71.86	7.04	[g]	71.86	6.94	
V[c]	176–177	Methanol		$C_{24}H_{28}N_5O_7$	58.41	4.70	14.20	58.68	4.79	13.75
VI	138–139	Toluene	95	$C_{18}H_{14}N_2O_3$			9.15			9.11
VII[c]	233–234	Dil methanol		$C_{17}H_{17}N_5O_7$	50.62	4.25	17.37	50.38	4.53	17.06

[a] Dinitrophenylhydrazone. [b] Lit.[3] bp 194–202° (0.2 mm). [c] Picrate. [d] Method A. [e] Method B. [f] Hydrochloride. [g] *Anal.* Calcd: Cl, 11.79. Found: Cl, 12.31.

methyl-2-nitrovinyl)indole in 50 ml of pyridine. The reaction was exothermic and a solid appeared. After standing overnight the mixture was diluted with cold water, and the precipitate was collected and dried.

Reduction of 12.2 g of VI with 10 g of $LiAlH_4$ in 400 ml of THF gave 2.5 g of a substance, bp 165–170° (2 mm), mp 100–102° (petroleum ether (bp 30–60°)–ethyl acetate), which was identified as *dl*-α-methyltryptamine (VII) by mixture melting point.

Acknowledgment.—We are indebted to Mr. H. G. McCann of the Microanalytical Laboratory, National Institute of Arthritis and Metabolic Diseases, for analyses.

Book Reviews

Survey of European Nonconventional Chemical Notation Systems. Edited by DONALD E. H. FREER. Publication No. 1278, National Academy of Sciences, National Research Council, Washington, D. C. 78 pp.

This is a 78 page addendum to the 467 page publication no. 1150 entitled, "Survey of Chemical Notation Systems," which appeared in 1964 and covered those systems in active use in the United States. Since this is a supplement to the original publication, it utilizes the terms and definitions given in publication no. 1150. It should be emphasized that to benefit from the European report, one must have a copy of the original report 1150. The definitions of terms and the historical summary given in publication 1150 represent an important step toward standardization in this complex and swiftly growing field, and anyone interested in following it should carefully study those sections of the original report.

The present publication serves as an excellent supplement to the original report, and the two reports cover all work being done in this field, with the exception of some efforts in the Soviet Union and Japan. Those involved with chemical information retrieval, including the storage of chemical structural information as well as properties, will need to study both of these reports. Those who are working in this area are keenly aware of the fact that none of us has been formally trained for this type of work. Therefore, careful study of such publications as these two surveys is absolutely mandatory for anyone who is trying to keep up with the field of chemical information retrieval.

SMITH KLINE AND FRENCH LABORATORIES PHILADELPHIA, PENNSYLVANIA — PAUL N. CRAIG

Clinical Pharmacology (Dilling). Edited by STANLEY ALSTEAD, J. GORDON MACARTHUR, THOMAS J. THOMSON, and W. FERGUSON ANDERSON, with 6 contributors. 21st ed. Baillière Tindall and Cassell, London; The Williams and Wilkins Co., Baltimore, Md., U. S. agents. 1965. xii + 741 pp. 14 × 19 cm. $8.00.

This is a standard text of pharmacology, of the older type, for undergraduate medical students, with only a measure of effort to present causative approaches to medical science on the level of molecular biology. The book carries useful descriptions of almost all the major drugs, and clinically well-founded recommendations for their use. The introductory chapters contain a modern version of Materia medica, but it is gratifying to see that the fundamentals of drug design and other topics in medicinal chemistry are presented, even though very briefly, to the budding pharmacologist. A section on the nomenclature of drugs is an extra bonus; however, it assumes that the second-year medical student has forgotten even the rudiments of organic chemistry and, therefore, reaches down to a quite primitive level. Prescription writing is taught well; an inadequate listing of insecticides appears to be out of place.

On the whole this book does not come up to the standard of the best American pharmacology texts.

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