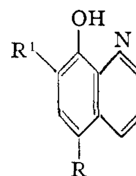
TABLE I

5-ACYL- AND 5-ALKYL-8-QUINOLINOLS



Compound No.	R	R[1]	M.p.,[a] °C.	Yield, %	Formula	Analyses,[b] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
I	Methyl[c]	Diethylaminomethyl	174	70	$C_{15}H_{20}N_2O\cdot HBr$	55.38	55.67	6.31	6.31
II	Methyl	4-Phenyl-1-piperazylmethyl	156	91	$C_{21}H_{23}N_3O$	75.65	75.96	6.95	7.30
III	Methyl	1-Piperidylmethyl[d]	268	97	$C_{16}H_{20}N_2O\cdot 2HBr$	45.95	46.24	5.34	5.35
IV	Methyl	4-Morpholinylmethyl	99	73	$C_{15}H_{18}N_2O_2$	69.74	69.76	7.02	7.30
V	Methyl	Ethyl-β-hydroxyethylaminomethyl	200	56	$C_{15}H_{20}N_2O_2\cdot 2HCl$	54.06	54.34	6.66	6.93
VI	Acetyl	1-Piperidylmethyl	208	67	$C_{17}H_{20}N_2O_2$	71.80[e]	71.72	7.09	7.36
VII	Ethyl	1-Piperidylmethyl	242	95	$C_{17}H_{22}N_2O\cdot HBr$	58.12	58.17	6.60	6.65
VIII	Benzoyl	1-Piperidylmethyl	251	81	$C_{22}H_{22}N_2O_2\cdot 2HBr$	51.98	52.24	4.76	5.11
IX	Benzyl	1-Piperidylmethyl	275	56	$C_{22}H_{24}N_2O\cdot 2HBr$	53.45	53.09	5.30	5.50
X	Pelargonyl		67	17[f]	$C_{18}H_{23}NO_2$	75.76	75.92	8.12	8.09
XI	Nonyl		217	16	$C_{18}H_{25}NO\cdot HBr$	61.31	61.27	7.44	7.57
XII	Palmitoyl		223	11	$C_{25}H_{37}NO_2\cdot HBr$	64.64	65.07	8.25	8.33
XIII	Palmitoyl	1-Piperidylmethyl	167	54	$C_{31}H_{48}N_2O_2\cdot HBr$	66.30	67.09	8.79	9.06
XIV	Hexadecyl[g]		63	63					

[a] Melting points are not corrected. Salts melt with decomposition. [b] Analyses are by Mr. Charles Childs and staff of these laboratories. [c] 5-Methyl-8-quinolinol was prepared by the method of E. Noelting and E. Trautmann, *Ber.*, **23**, 3666 (1890). [d] 1-Phenylpiperazine was supplied by Dr. Robert F. Parcell of these laboratories. [e] Calcd.: N, 9.85. Found: N, 10.04. [f] Yield based on hydrochloride. [g] Although an analytical sample could not be obtained, the characteristic infrared absorption band of the ketone moiety is missing.

After 20 hours at room temperature, the dark mixture was decomposed carefully with a slurry of dilute hydrochloric acid and ice. The nitrobenzene was steam distilled. The thick residue was neutralized with strong alkali until faintly acid to *p*H paper. The filtered reaction mass was extracted with several portions of acetone. The acetone solution was saturated with hydrogen bromide to yield 19 g. (17%) of yellow solid, m.p. 229–231° (dec.).

For analysis, a sample was converted to the free base by neutralizing an aqueous suspension with alkali extracting the dried solid with ether and recrystallizing the light brown crystals several times from ethanol; m.p. 66–67°.

The similar pentadecyl ketone (XII) was prepared in like manner. The ketones were reduced catalytically by the method of K. Rosenmund and G. Karst.[3]

5-Acyl- and 5-Alkyl-7-dialkylaminomethyl-8-quinolinols.—A previously heated solution of molar equivalents of amine and paraformaldehyde in ethanol was added to a solution of the quinolinol in ethanol. After a brief reflux period (1–2 hours), the solution was either concentrated and cooled to separate the product or diluted with dry ether and acidified with dry hydrogen bromide gas to separate the salt. The solid was then purified by several recrystallizations from ethanol or isopropyl alcohol.

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Additional Evidence on the Enzymatic Transformation of Histidine into Glutamic Acid

BY J. P. FOURNIER AND L. P. BOUTHILLIER

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By the use of heavy nitrogen as a tracer element, Tabor and his collaborators[1] demonstrated conclusively that the γ-nitrogen of histidine appears in the amino group of the glutamic acid resulting from the enzymatic degradation of the former. They have also presented direct evidence that the initial step in the breakdown of histidine is its deamination to the formation of urocanic acid. Their findings are thus in agreement with the theory formulated by Sera and his co-workers,[2] Takeuchi[3] and Oyamada,[4] whereby histidine would be biologically degraded to urocanic acid, formylisoglutamine, isoglutamine and glutamic acid.

We wish to report here some experimental data which provide additional support to the above theory. Freshly prepared liver homogenates were incubated in presence of carboxyl-C^{14}-labeled DL-histidine. Two-dimensional paper partition chromatograms (solvent mixtures: water-saturated-phenol + HCN + 0.3% NH_3 and water-saturated *n*-BuOH + glacial AcOH) of the original incubation mixtures, as compared to incubation blanks without histidine, revealed upon treatment with ninhydrin the marked intensification of only one spot, that corresponding to glutamic acid. The latter was further identified by the mixed spot technique. The biologically formed glutamic acid was then isolated with carrier, and recrystallized several times to constant radioactivity in the form of its calcium salt. Samples of the regenerated glutamic acid were decarboxylated (α-COOH) by treatment with ninhydrin and the activity of the evolved carbon dioxide was measured. The results appear in Table I. Since our data indicate that only a small fraction of the total activity contained in the glutamic acid was present in the α-carboxyl group of the molecule, it seems reasonable to assume that the radioactivity was concentrated almost entirely in the γ-carboxyl carbon. The conclusion is reached that the α- and γ-carboxyl carbons of the

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(2) K. Sera and S. Yada, *J. Osaka Med. Soc.*, **38**, 1107 (1939); K. Sera and D. Aihara, *ibid.*, **41**, 745 (1942).

(3) M. Takeuchi, *J. Biochem.* (*Japan*), **34**, 1 (1941).

(4) Y. Oyamada, *ibid.*, **36**, 227 (1944).

glutamic acid originate, respectively, from the δ and carboxyl carbons of its precursor histidine. Thus our results are consistent with the proposed pathway[2-4] for histidine metabolism and confirm the findings of Tabor, *et al.*[1]

TABLE I

Experiment No.	Specific activity of glutamic acid, counts per min. per mM.	Specific activity of ninhydrin-liberated CO_2 (α-COOH), counts per min. per mM.	C^{14} in α-COOH carbon of glutamic acid, %
1A	4100	170	4.2
1B	4100	188	4.6
2A	5220	125	2.4
2B	5220	133	2.6

Experimental

Radioactive Histidine.—DL-Histidine dihydrochloride labeled with C^{14} on the carboxyl carbon position was synthesized.[5] Its activity was measured with the use of a thin mica window tube and corresponded to approximately 1100 counts per minute per mg.

Incubation of Liver Homogenates in Presence of Labeled Histidine.—Cell-free homogenates of rat liver were prepared.[6] Into each of 50-ml. conical flasks were added 25 mg. of DL-histidine ($C^{14}OOH$)·2HCl, 1 ml. of 0.22 N NaOH to neutralize the hydrochloric acidity, 5-ml. aliquots of fresh homogenate and finally 10 mg. of normal L-glutamic acid as trapping agent, in the case of experiments 2A and 2B. The flasks were stoppered with cotton plugs and then agitated for 6 hours in a 38° water-bath.

Isolation and Purification of Glutamic Acid.—At the end of the incubation period, the contents of each flask were mixed with 10 volumes of absolute alcohol and heated to boiling for 10 minutes. The coagulated protein was separated by centrifugation and washed twice with alcohol. The clear alcohol solutions and washings of each preparation were evaporated to about 1 ml. and the volume brought to 10 ml. with distilled water. Into each solution was added as carrier 300 mg. of L-glutamic acid. Glutamic acid was precipitated as the calcium salt, recrystallized three times in water and alcohol, and regenerated according to the method of Foreman.[7] The aqueous solutions were each concentrated to about 4 ml. to which was added 10 ml. of absolute alcohol. Glutamic acid was allowed to crystallize slowly in an ice-box. Quantities of the purified radioactive amino acid as large as 150 mg. were recovered.

Decarboxylation of Glutamic Acid and Radioactivity Measurements.—Fifty-mg. portions of isotopic glutamic acid were decarboxylated by means of ninhydrin[8] and the evolved carbon dioxide was collected as barium carbonate. The radioactivity of the glutamic acid and the barium carbonate (40-mg. samples each) was measured with a thin mica window Geiger counter, corrected for background and self-absorption.[9] The final values were expressed as counts per minute per millimole.

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Solubility of Diborane- and Boron-containing Lithium Salts[1]

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As part of a program for studying the preparation of diborane from lithium hydride and boron trihalides in ether type solvents, it became necessary for us to determine the approximate solubility of diborane and several boron-containing lithium salts in the two solvents, diethyl ether and tetrahydrofuran.

The solubility of diborane gas was calculated from measurements of the pressure of the vapor in equilibrium with a solution of diborane at various temperatures. The temperature–pressure data listed in Tables I and II were interpreted by assuming perfect gas laws and estimating the vapor

TABLE I

EQUILIBRIUM PRESSURES FOR DIBORANE IN DIETHYL ETHER

Weight diethyl ether, 20.24 g.; volume of cylinder, 79.3 cc.

Series A 0.395 g. diborane Temp., °C.	Obsd. press., p.s.i. abs.	Series B 0.617 g. diborane Temp., °C.	Obsd. press., p.s.i. abs.	Series C 1.032 g. diborane Temp., °C.	Obsd. press., p.s.i. abs.
0.5	21.7	0.6	28.7	0.8	54.7
11.3	27.7	12.0	41.2	13.0	60.7
27.2	37.7	24.5	51.2	25.5	74.7
40.3	49.2	40.0	67.7	40.0	94.7
58.3	69.7	60.0	95.7	50.0	111.7
27.0	38.2				

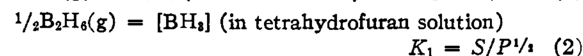
TABLE II

EQUILIBRIUM PRESSURES FOR DIBORANE IN TETRAHYDROFURAN

Wt. diborane, g.	0.540	1.008	1.721	0.993	1.704	2.172
Wt. tetrahydrofuran, g.	25.01	25.01	25.01	24.18	24.18	24.18
Vol. of cylinder, cc.	79.3	79.3	79.3	76.3	76.3	76.3
T, °C.	Observed pressure, p.s.i. abs.					
7	2.9	3.2	4.9	2.9	5.9	13.2
20	3.9	5.6	9.8	5.4	12.2	26.7
30	5.9	9.1	16.7	9.3	21.7	42.7
40	8.3	15.2	27.7	14.2	32.7	66.7
50	...	21.5	42.2	...	49.7	93.7

pressure of the solvent on the basis of Raoult's law. The equilibrium partial pressures of solute were obtained by difference, using successive approximations for the lowering of the vapor pressure of the solvent by the solute. Calculations are summarized in Tables III and IV in terms of the equilibria

$$B_2H_6(g) = B_2H_6 \text{ (in ether solution)} \qquad K_1 = S/P \qquad (1)$$



$$1/2 B_2H_6(g) = [BH_3] \text{ (in tetrahydrofuran solution)} \qquad K_1 = S/P^{1/2} \qquad (2)$$

where P is the equilibrium pressure of diborane in atmospheres and S is the solubility expressed as moles diborane in 100 g. of solvent.

(1) This work was done on U. S. Army Ordnance Contract No. TUI-2000.