linear concentration gradient, which leads to the parabolic law, the concentration of diffusion species would decrease exponentially along the diffusion paths, or

$$c = c_0e^{-\alpha x}$$

where c is the concentration of the diffusion species at a distance x from its starting point. Thus, the concentration gradient would be

$$\partial c/\partial x = -c_0ke^{-\alpha x}$$

Since the total thickness of oxide, x, is related to the amount of substance that has diffused, w, by a gravimetric factor $w = gx$, then

$$dw/dt = -Dc_0\alpha e^{-w\alpha/g}$$

Integrating

$$w = k \log(1 + at)$$

which is the logarithmic law for oxidation.

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NOTES

Quaternary Salts of Halogenated Pyridines and Quinolines[1]

BY CARL T. BAHNER, WM. K. EASLEY, MADGE D. PICKENS, HAROLD D. LYONS, LILBURN L. NORTON, BETTY GAY WALDEN AND GEORGE E. BIGGERSTAFF

Since certain quaternary salts of pyridine and quinoline have been reported to damage sarcoma cells *in vivo*[2] we have prepared similar salts of several halogenated pyridines and quinolines for screening against sarcoma in mice[3] and for correlation of biological effects and other properties with structure.

The quaternary salts listed in Tables I and II were prepared by reaction of a halogenated heterocyclic base with the appropriate organic halide at 30–40°. When the reactants alone did not form a homogeneous solution a small amount of chloroform was added to bring them into solution. The products usually precipitated as they were formed and the mixture was allowed to stand as long as seemed necessary to obtain a good yield. The rates of reaction varied greatly. For 6-chloroquinoline the reaction periods were: with glycerol-

TABLE I

HALOPYRIDINE DERIVATIVES

Salt from	Empirical formula	M.p., °C.[a]	Analyses, % Ionic Halogen Calcd.	Found[b]
2-Chloropyridine and				
β-Phenylethyl bromide	$C_{13}H_{13}BrClN$	193	26.76	26.50
Styrene bromohydrin	$C_{13}H_{13}BrClNO$	182	25.40	25.30
Phenacyl bromide	$C_{13}H_{11}BrClNO$	187	25.57	25.30
p-*t*-Butylphenacyl bromide	$C_{17}H_{19}BrClNO$	192	21.68	21.40
p-Fluorophenacyl bromide	$C_{13}H_{10}BrClFNO$	185–187	24.17	24.03
p-Chlorophenacyl bromide	$C_{13}H_{10}BrCl_2NO$	188–189	23.03	23.01
p-Bromophenacyl bromide	$C_{13}H_{10}Br_2ClNO$	194	20.41	20.42
p-Iodophenacyl bromide	$C_{13}H_{10}BrClINO$	193	18.23	18.00
m-Nitrophenacyl bromide	$C_{13}H_{10}BrClN_2O_3$	172	22.35	22.42
2-Bromopyridine and				
p-Fluorophenacyl bromide	$C_{13}H_{10}Br_2FNO$	174–175	21.30	21.08
p-Chlorophenacyl bromide	$C_{13}H_{10}Br_2ClNO$	201	20.41	20.44
p-Iodophenacyl bromide	$C_{13}H_{10}Br_2INO$	189	16.55	16.40
p-Phenylphenacyl bromide	$C_{19}H_{15}Br_2NO$	160–161	18.45	18.54
5,6,7,8-Tetrahydro-β-naphthacyl bromide	$C_{17}H_{17}Br_2NO$	207	19.44	19.54
3-Fluoropyridine and				
p-Fluorophenacyl bromide	$C_{13}H_{10}BrF_2NO$	189	25.36	25.29
3-Chloropyridine and				
p-Fluorophenacyl bromide	$C_{13}H_{10}BrClNO$	169–170	24.17	24.33

(1) This investigation was supported in part by a research grant from the National Cancer Institute, of the National Institutes of Health, Public Health Service.

(2) Shear, *et al.*, in "Approaches to Cancer Chemotherapy," American Association for the Advancement of Science, F. R. Moulton, Editor, Washington, D. C., 1947, p. 236 ff.; *cf.* J. L. Hartwell and S. R. L. Kornberg, THIS JOURNAL, **68**, 1131 (1946).

(3) Results of screening tests at the National Cancer Institute are to be reported elsewhere.

TABLE I (*Continued*)

	Empirical formula	M.p., °C.[a]	Analyses, % Ionic Halogen Calcd.	Found[b]
3-Bromopyridine and				
Decyl iodide	$C_{15}H_{25}BrIN$	80	29.77	29.92
2,5-Diiodohexane (bis-salt)	$C_{16}H_{20}I_4N_2$	244–245	38.93	38.83
Glycerol-α,γ-dibromohydrin	$C_{13}H_{14}Br_4N_2O$	330	29.93	29.83
Ethyl iodoacetate	$C_9H_{11}BrINO_2$	178–179	34.12	34.53
Cyclohexylethyl bromide	$C_{13}H_{19}Br_2N$	123–125	22.90	22.96
Styrene bromohydrin	$C_{13}H_{13}Br_2NO$	216–217	22.25	22.51
p-*t*-Butylphenacyl bromide	$C_{17}H_{19}Br_2NO$	210–211	19.34	19.64
2,5-Dimethylphenacyl bromide	$C_{15}H_{15}Br_2NO$	254	20.75	20.73
p-Fluorophenacyl bromide	$C_{13}H_{10}Br_2FNO$	112	21.28	20.97
p-Chlorophenacyl bromide	$C_{13}H_{10}Br_2ClNO$	236–240	20.40	20.41
p-Iodophenacyl bromide	$C_{13}H_{10}Br_2INO$	268–270	16.55	16.57
2,5-Dichlorophenacyl bromide	$C_{13}H_9Br_2Cl_2NO$	238–239	18.76	18.74
m-Nitrophenacyl bromide	$C_{13}H_{10}Br_2N_2O_3$	207–209	19.87	19.73
3,4-Dihydroxyphenacyl bromide	$C_{13}H_{11}BrClNO_3$	252	[c]	
p-Methoxyphenacyl bromide	$C_{14}H_{13}Br_2NO_2$	243	20.64	20.64
β-Naphthacyl bromide	$C_{17}H_{13}Br_2NO$	234–235	19.63	19.29
β-Naphthacyl iodide	$C_{17}H_{13}BrINO$	214–215	27.95	27.76
anti-β-Naphthacyl iodide oxime	$C_{17}H_{14}BrIN_2O$	202–203	[d]	
4-Fluoro-α-naphthacyl bromide	$C_{17}H_{12}Br_2FNO$	214	18.80	18.52
5,6,7,8-Tetrahydro-β-naphthacyl bromide	$C_{17}H_{17}Br_2NO$	220–221	19.44	19.24
α-Bromo-β-propionaphthone	$C_{18}H_{15}Br_2NO$	234–235	18.98	18.83
p-Chlorophenyl-α-bromoethyl ketone	$C_{14}H_{12}Br_2ClNO$	203–204	19.71	19.57
3-Iodopyridine and				
2,5-Diiodohexane	$C_{16}H_{20}I_4N_2$	261–264	34.02	34.03
p-Fluorophenacyl bromide	$C_{13}H_{10}BrFINO$	202–204	18.98	19.08
3,5-Dibromopyridine and				
Decyl iodide	$C_{15}H_{24}Br_2IN$	208–209	15.82	15.95
β-Phenylethyl iodide	$C_{13}H_{13}Br_2IN$	206–207	27.01	27.13
p-*t*-Butylphenacyl bromide	$C_{17}H_{18}Br_3NO$	190–191	16.24	15.93
p-Fluorophenacyl bromide	$C_{13}H_9Br_3FNO$	220	17.60	17.36
p-Chlorophenacyl bromide	$C_{13}H_9Br_3ClNO$	225–226	16.98	17.21
p-Bromophenacyl bromide	$C_{13}H_9Br_4NO$	227–228	15.52	15.64
p-Iodophenacyl bromide	$C_{13}H_9Br_3INO$	237	14.22	14.48
m-Nitrophenacyl bromide	$C_{13}H_9Br_3N_2O_3$	238	16.62	16.40
p-Methoxyphenacyl bromide	$C_{14}H_{12}Br_3NO_2$	251	17.15	17.15
p-Chlorophenyl-α-bromoethyl ketone	$C_{14}H_{11}Br_3ClNO$	192	16.50	16.51
p-Phenylphenacyl bromide	$C_{19}H_{14}Br_3NO$	216–217	15.60	15.80
β-Naphthacyl bromide	$C_{17}H_{12}Br_3NO$	203–204	16.44	16.19
β-Naphthacyl iodide	$C_{17}H_{12}Br_2INO$	180–181	23.81	23.99
5,6,7,8-Tetrahydro-β-naphthacyl bromide	$C_{17}H_{16}Br_3NO$	231–232	16.30	16.40
5,6,7,8-Tetrahydro-β-naphthacyl iodide	$C_{17}H_{16}Br_2INO$	205	23.62	23.78

[a] Salts melted with decomposition. [b] Average of two Volhard analyses, unless otherwise indicated. [c] Calcd.: C, 45.32; H, 3.22. Found: C, 45.26; H, 3.48. [d] Calcd.: C, 43.53; H, 3.01. Found: C, 43.46; H, 3.12.

α,γ-dibromohydrin[4] 60 days, with decyl iodide[4] 14 days, with β-phenylethyl bromide[4] 18 days, with β-phenylethyl iodide[4] 18 hours, with phenacyl bromide[5] 14 days, with *p*-methoxyphenacyl bromide[5] 4 days, with *p*-iodophenacyl bromide[5] 24 hours and with β-naphthacyl bromide[5] 24 hours. Among the bases, 3,5-dibromopyridine and 3-bromopyridine reacted more rapidly than 2-chloropyridine and 2-bromopyridine, while 4,7-dichloroquinoline reacted much less rapidly than 6-chloroquinoline. The results observed were in line with the expected deactivating effect of a negative atom attached at the 2- or 4- position on the heterocyclic ring and the steric hindering by a large atom or group attached to the carbon adjacent to the nitrogen.

The bromide salts were white or cream solids while the iodides were yellow. Some of those with low molecular weights were very soluble in water, while others were only slightly soluble. Most of the salts were recrystallized by dissolving in warm methanol, ethanol or ethyl acetate and adding isopropyl ether, but some were recrystallized from water, alcohol or acetone without the aid of isopropyl ether.

(4) Without solvent.

(5) In chloroform.

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TABLE II

HALOQUINOLINE DERIVATIVES

Salt from 6-chloroquinoline and	Empirical formula	M.p., °C.	Analyses, % Ionic halogen Calcd.	Found
Decyl iodide	$C_{19}H_{27}ClIN$	113	29.39	29.33
Glycerol-α,γ-dibromohydrin	$C_{12}H_{12}Br_2ClNO$	234	20.95	21.22
β-Cyclohexylethyl bromide	$C_{17}H_{21}BrClN$	102	22.52	22.33
β-Phenylethyl bromide	$C_{17}H_{15}BrClN$	108–111	22.92	22.83
β-Phenylethyl iodide	$C_{17}H_{15}ClIN$	164	32.09	31.90
Phenacyl bromide	$C_{17}H_{13}BrClNO$	215	22.04	21.78
p-*t*-Butylphenacyl bromide	$C_{21}H_{21}BrClNO$	232	19.08	18.98
p-Chlorophenacyl bromide	$C_{17}H_{12}BrCl_2NO$	205	20.12	20.12
p-Bromophenacyl bromide	$C_{17}H_{12}Br_2ClNO$	207	18.09	18.11
m-Nitrophenacyl bromide	$C_{17}H_{12}BrClNO_3$	215	19.60	19.52
p-Methoxyphenacyl bromide	$C_{18}H_{15}BrClNO$	211	20.34	30.33
β-Naphthacyl bromide	$C_{21}H_{15}BrClNO$	236.5	19.37	19.43
5,6,7,8-Tetrahydro-β-naphthacyl bromide	$C_{21}H_{19}BrClNO$	252	19.17	18.95
3-Bromoquinoline and				
p-Fluorophenacyl bromide	$C_{17}H_{12}Br_2FNO$	258	18.80	18.84

samples of 3-fluoro, 3-chloro and 3-iodopyridine, and to Miss Emogene Stephen, Miss Carolyn Cate, Mr. Tom Fuller and Mr. Lynn Easley for assistance in the purification of the products.

DEPARTMENT OF CHEMISTRY
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Color Reactions of Human Antibody and Normal Human Gamma Globulin[1]

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As a criterion of purity of the blood group A substances[2,3,4,5] determinations were carried out of the proportions of two characteristic constituents of these antigens, hexosamine and methylpentose, specifically precipitated by an excess of antibodies to A substance. Since such specific precipitates consist of both antigen and antibody, total color values for hexosamine[6] and methylpentose[7] in specific precipitates must be corrected for any color given in these reactions by the antibody. The equivalent color values of normal human γ-globulin were used for this purpose although the possibility was recognized[2] and commented upon[8] that human antibody and normal human gamma globulin may not give identical color values. This report shows that human antipneumococcal antibodies give color values identical with those for human gamma globulin in the reactions for hexosamine and methylpentose as well as with Folin–Ciocalteu tyrosine reagent.[9]

Experimental

Antipneumococcal antibodies were produced by injection into a human being of a mixture of pneumococcal polysaccharides.[10] A large sample of serum was obtained and found to contain 38 μg. anti-C[11], 23 μg. anti-SII[11] and 9 μg. anti-SIII[11] N per ml. Specific precipitates of C-anti-C, SIII-anti-SIII and SII-anti-SII were obtained from about 100-ml. portions of serum, which had been in the refrigerator until the complement was destroyed, washed free from excess serum protein[9,10,12] dissolved in water with 0.5 ml. of 0.1 *M* NaOH, and made up to a known volume. Four samples of normal human gamma globulin were available for comparison with the human antibodies.[13]

Hexosamine/Total N Ratio.—Aliquots of the dissolved SII-anti-SII and SIII-anti-SIII specific precipitates were analyzed for nitrogen by the Markham micro-Kjeldahl method[14,12] and for hexosamine by a modification[15] of the Elson-Morgan procedure.[6] The hexosamine values were corrected for the color given in this reaction by the SII and SIII in the dissolved precipitates; these samples of polysaccharide gave color values equivalent to 3.3 and 0.9% hexosamine, respectively. Two lots of normal human gamma globulin were analyzed for nitrogen and hexosamine. C-anti-C precipitates were not suitable for determining the hexosamine/total N ratio since the C substance has a high (22%) hexosamine content.

Methylpentose/Total N Ratio.—SIII-anti-SIII and C-anti-C specific precipitates and three gamma globulin samples were analyzed for methylpentose and nitrogen,[14] and the values for the specific precipitates corrected for the methylpentose color given by these polysaccharides; SIII and C gave color values equivalent to 1.4 and 0.8% methylpentose, respectively. SII-anti-SII specific precipitates were not used in determining the methylpentose/N ratios since the SII sample contained 40% of methylpentose.

Folin–Ciocalteu Color Equivalent.—SII-anti-SII and SIII-anti-SIII specific precipitates and two gamma globulin samples were used. SII and SIII contain no nitrogen and give no color with the Folin–Ciocalteu tyrosine reagent and no correction for their presence in the precipitates was necessary. Appropriate dilutions of known nitrogen content were analyzed as described by Heidelberger and MacPherson.[9,12] Color development at 7500 Å. was proportional to N up to about 25 μg. N.

The values of hexosamine/N, methylpentose/N and mean

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