TABLE I

PHYSICAL CONSTANTS

Aromatic hydrocarbon	F. p., °C.	B. p., 760 mm., °C.	Density, g./ml. at 20°C.	$n^{20}D$
Benzene[a]	+ 5.50	80.08	0.8789	1.5011
Toluene[a]	−95.01	110.58	.8670	1.4967
Ethylbenzene[a]	−95.01	136.25	.8671	1.4958
n-Propylbenzene[c]	−99.57	159.31	.8618	1.4919
Isopropylbenzene[a]	−96.02	152.42	.8619	1.4912
o-Xylene[b]	−25.22	144.41	.8798	1.5052
p-Xylene[b]	+13.28	138.36	.8608	1.4958
m-Diethylbenzene[a]	−84.09	181.62	.8641	1.4955
p-Cymene[a]	−68.17	177.23	.8567	1.4908
1,3,5-Triethylbenzene[d]	−66.48	215.92	.8621	1.4958
3,5-Diethyltoluene[e]	−74.12	200.70	.8631	1.4969

[a] Commercial product purified by distillation through 100 theoretical plate columns. [b] Purified by low-temperature fractional crystallization as well as distillation. [c] Synthesized according to H. Gilman and W. E. Catlin in Gilman, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1941, Coll. Vol. I, 2nd ed., p. 471, and purified by distillation. [d] Prepared according to W. B. Dillingham and E. E. Reid, THIS JOURNAL, **60**, 2606 (1938), except that ethylbenzene was used instead of benzene. It was also purified by distillation. [e] Prepared by the ethylation of toluene according to J. F. Norris and D. Rubinstein, THIS JOURNAL, **61**, 1163 (1939), except that the ethylation was run at room temperature. Ethyl bromide was used in both ethylations.

fractometer and the method of density determination were checked by the use of National Bureau of Standards sample of toluene, No. 211a.

NATIONAL ADVISORY COMMITTEE FOR AERONAUTICS
AIRCRAFT ENGINE RESEARCH LABORATORY
CLEVELAND, OHIO

RECEIVED JANUARY 23, 1946

Improved Preparation of Creatinine Zinc Chloride

BY WM. A. PEABODY

The preferred process for making creatinine zinc chloride has been the fusion method of Edgar and Hinegardner.[1] Its advantage, the adequacy of technical creatine as a raw material, is offset by relatively poor yield, the need for recrystallization, and occasional difficulty in controlling the fusion (particularly with larger batches.) Inspection of their recrystallization procedure led to the conclusion that the synthesis should result satisfactorily by simple metathesis between creatinine hydrochloride and zinc acetate in water. Preliminary trials proved this to be the case; primary yields were high, and quality under properly controlled conditions was equal to that of the recrystallized product of the fusion method.

Procedure.—Combine in the proportions 500 g. of dry creatinine hydrochloride and 367 g. of C. P. zinc acetate dihydrate, dissolved separately in approximately 310 cc. and 750 cc. of hot distilled water in 2 and 1.5 liter beakers, respectively. Since final concentrations are near saturation, make small water additions as needed to replace evaporation losses until solutions are complete. Stir the hydrochloride solution while pouring the acetate solution into it fairly rapidly, followed by a little wash water. Cool promptly in tap water, then chill to about 0°. Filter by suction, wash with one or two small portions of 70–80% methanol or ethanol, then with 99.5% methanol until acetic odor is faint or absent, and dry; yield, 545–560 g. of white product (90–92.5%). A second crop of about 13 g., obtained by chilling the filtrate after addition of 1–1.5 volumes of methanol, requires recrystallization from acetic acid[1] to reach analytical purity.

The creatinine hydrochloride need not be white, but should not be more than slightly yellow or greenish-yellow. When the hydrochloride is available, the present method is a great saver of time and materials. If one must begin with technical creatine, the choice between the two methods may be a matter of personal preference. Conversion of creatine[1,2] to a good grade of creatinine hydrochloride is not particularly difficult, but does take some time and effort. With experience, one presumably should be able to omit final crystallization of the hydrochloride if its concentrated solution is sufficiently pure and its concentration determined with moderate accuracy. The use of concentrated reactant solutions eliminates the need of alcohol at the precipitation stage, which, together with acetic acid formation, minimizes co-precipitation of any excess reactant or dissolved impurities.

The author is indebted to Mrs. Ruth H. Powell, Miss Alice Parson and Mr. W. J. Martin for a number of the analyses.

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[1] Edgar and Hinegardner, "Organic Syntheses," Coll. Vol. I, 2d ed., John Wiley and Sons, Inc., New York, N. Y., 1941, pp. 173, 172.

[2] Hunter, "Creatine and Creatinine," Longmans, Green and Co., Ltd., London, 1928, pp. 54–55.

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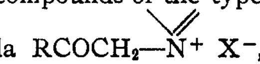
RECEIVED MARCH 28, 1946

Some Quaternary Ammonium Salts of Heterocyclic Bases. II[1,2]

BY JONATHAN L. HARTWELL AND SYLVIA R. L. KORNBERG

The biological results obtained by our collaborators[3] on compounds of the type represented by the formula  $RCOCH_2—\overset{\diagdown\!\!\diagup\!\!\diagup}{N}^+ X^-$, where the nitrogen atom is the hetero atom in an aromatic base of the type of pyridine and its homologs or benzologs,[4] warranted the preparation of other series of related quaternary ammonium salts. For this purpose, two series were prepared, in which R was α-naphthyl and β-naphthyl, respectively. These compounds were formed by the addition of the appropriate naphthacyl bromide to the base, except in the case of the 1-(α-naphthacyl)-3-picolinium and 1-(α-naphthacyl)-3-methylisoquinolinium halides where difficulty was encountered in obtaining the bromides pure. In these two instances, iodides were then prepared by both the ionic reaction of the bromides with potassium

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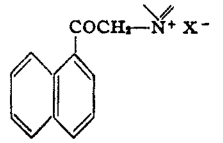
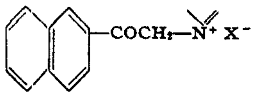
[1] Paper XIII in the series entitled "Chemical Treatment of Tumors." Paper XII in this series: Hartwell and Kornberg, THIS JOURNAL, **68**, 868 (1946).

[2] Material contained in this paper was presented, in part, at the meeting of the American Association for Cancer Research at Atlantic City, N. J., March 11, 1946. Abstract in *Cancer Research*, **6**, in press (1946).

[3] Peters, Hartwell, Dalton and Shear; Dalton and Peters, *ibid.*, **6**, in press (1946).

[4] Hartwell and Kornberg, ref. 1.

TABLE I

Compound	Base used	X	Appearance	M. p., °C., cor.[a]	Yield, crude, %	Empirical formula	Analyses,[b] %: Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
										
1[c]	Pyridine	Bromide	Pale yellow prisms	235.2–236.2 (dec.)	38	$C_{17}H_{14}BrNO$	62.2	62.1	4.3	4.6
2	α-Picoline	Bromide	White prisms	227.0–227.7 (dec.)	33	$C_{18}H_{16}BrNO$	63.2	63.0	4.7	4.8
3	β-Picoline	Iodide	Yellow needles	218.6–219.5 (dec.)	21[i]	$C_{18}H_{16}INO$	55.5	55.6	4.1	4.5
4	γ-Picoline	Bromide	Pale buff needles	243.0–243.8 (dec.)	42	$C_{18}H_{16}BrNO$	63.2	63.2	4.7	4.9
5	Quinoline	Bromide	Yellow needles	240.1–240.9 (dec.)	22	$C_{21}H_{16}BrNO$	66.7	66.5	4.3	4.6
6	Isoquinoline	Bromide	Buff needles	267.4–267.7 (dec.)	50	$C_{21}H_{16}BrNO$	66.7	67.0	4.3	4.4
7	3-Methylisoquinoline	Iodide	Yellow prisms	189.9–190.6 (darkens)	69[e]	$C_{22}H_{18}INO$	60.1	59.7	4.1	4.4
8	3-Methylisoquinoline	Picrate	Yellow prisms	212.2–214.2	98[f]	$C_{28}H_{20}N_4O_8$	62.2	62.2	3.7	3.9[g]
										
9[d]	Pyridine	Bromide	Light yellow prisms	219.3–220.2 (darkens)	88	$C_{17}H_{14}BrNO \cdot H_2O$	59.0	59.2[h]	4.7	4.6[h]
10	α-Picoline	Bromide	White plates	212.2–213.4 (darkens)	80	$C_{18}H_{16}BrNO \cdot H_2O$	60.0	60.0	5.0	5.1
11	β-Picoline	Bromide	White needles	243.6–244.4 (darkens)	85	$C_{18}H_{16}BrNO$	63.2	63.3	4.7	5.3
12	γ-Picoline	Bromide	Yellow prisms	254.0–254.7 (darkens)	78	$C_{18}H_{16}BrNO$	63.2	63.4	4.7	5.0
13	Quinoline	Bromide	Yellow plates	243.0–244.6 (darkens)	67	$C_{21}H_{16}BrNO$	66.7	66.5	4.3	4.5
14	Isoquinoline	Bromide	Buff globular aggregates	262.6–263.6 (dec.)	82	$C_{21}H_{16}BrNO$	66.7	66.5	4.3	4.1
15	3-Methylisoquinoline	Bromide	Pale yellow plates	241.4–242.7 (dec.)	76	$C_{22}H_{18}BrNO \cdot {}^3/_4H_2O$	65.1	65.2	4.8	4.8
16	3-Methylisoquinoline	Perchlorate	White prisms	217.1–218.3 (dec.)	92	$C_{22}H_{18}ClNO_5$	64.2	64.5	4.4	4.5

[a] All melting points were determined with the Hershberg apparatus, *Ind. Eng. Chem., Anal. Ed.*, **8**, 312 (1936). [b] The microanalyses were performed by Arlington Laboratories, Fairfax, Va., except where noted. [c] Kröhnke, *Ber.*, **69**, 933 (1936); m. p. 208–209° (dec.). No analysis reported. [d] Kröhnke, *Ber.*, **69**, 921 (1936); m. p.. 213°. No analysis reported. [e] Based on bromide. [f] Based on iodide. [g] Nitrogen analysis on this compound is: Calcd. for N, 10.4; found, 10.4. [h] Microanalyses performed by Mr. C. A. Kinser, National Institute of Health. [i] Prepared by the method of King (see ref. 5).

TABLE II

OXIMES

Compound	Prepared from compound no.	Appearance, white	M. p. °C., cor.[a]	Yield crude, %	Empirical formula	Analyses,[b] %: Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
17	9	Prisms[c]	251.9–253.4 (dec.)	93	$C_{17}H_{15}BrN_2O$	59.5	59.8	4.4	4.6	8.2	8.1
18	10	Crystalline aggr.[d]	233.7–234.4 (dec.)	24	$C_{18}H_{17}BrN_2O \cdot {}^3/_4H_2O$	58.3	58.4	5.0	5.0	7.6	7.7
19	14	Needles[d]	243.4–243.9 (dec.)	7	$C_{21}H_{17}BrN_2O$	64.1	63.7	4.4	4.6	7.1	7.3

[a] All melting points were determined with the Hershberg apparatus. [b] The microanalyses were performed by Arlington Laboratories, Fairfax, Va. [c] Crystallized from water. [d] Crystallized from alcohol.

iodide and by the method of King[5] using methyl α-naphthyl ketone, iodine, and the appropriate base.

Intermediates.—Methyl α-naphthyl ketone, methyl β-naphthyl ketone and the heterocyclic bases were obtained from commercial scources. α-Naphthacyl bromide and β-naphthacyl bromide were prepared by a method described in the literature.[6]

The Quaternary Ammonium Bromides.—The bromides were prepared by warming on the steam-bath a mixture of equivalent amounts of α- or β-naphthacyl bromide and the base for periods from a few minutes to one-half hour, and crystallizing from alcohol. Pure compounds could not be obtained from the reaction of α-naphthacyl bromide with β-picoline and with 3-methylisoquinoline. With β-picoline, gummy yellow crystals were obtained, in 44% yield, from which a product with a constant melting point could not be obtained by crystallization. With 3-methylisoquinoline, orange or pink crystals were obtained, in 28% yield, different samples melting at 157° or above over wide ranges.

The Quaternary Ammonium Iodides.—The two impure bromides mentioned were treated in aqueous solution with an excess of potassium iodide solution. 1-(α-Naphthacyl)-3-picolinium bromide gave a crude iodide in 59% yield, from which was isolated a pure crystalline iodide in poor yield after several crystallizations from alcohol. 2-(α-Naphthacyl)-3-methylisoquinolinium bromide gave a product in nearly theoretical yield from which could be obtained by crystallization from alcohol two preparations of yellow crystals melting, respectively, at 189.9–190.6° (darkens) cor. and 214.0–214.8° (dec.) cor.

The method of King[5] for the preparation of these iodides, using methyl α-naphthyl ketone, iodine and the appropriate bases, was also employed. This resulted in an improved procedure for 1-(α-naphthacyl)-3-picolinium iodide. In the case of 2-(α-naphthacyl)-3-methylisoquinolinium iodide, however, a gummy brown product was obtained in 71% yield, from which apparently constant melting yellow crystalline preparations could be obtained in small yield, the lowest-melting melting at 188.0–189.0° (darkens) cor. and the highest-melting melting at 220.8–221.5° (dec.) cor. The two preparations, of melting points just recorded, yielded crystalline picrates when treated with picric acid in alcohol solution. When recrystallized from alcohol, the picrate from the lower melting preparation melted at 212.2–214.2° cor. and yielded analytical values close to the theoretical. Although a homogeneous 3-methylisoquinolinium iodide was not obtained by either method tried, both the highest and lowest melting fractions

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(5) King, THIS JOURNAL, **66**, 894 (1944).

(6) Radcliffe, Sherwood and Short, *J. Chem. Soc.*, 2293 (1931).

mentioned above gave similar analytical values, close to the theoretical, for carbon and hydrogen, and all fractions of the iodide gave copious precipitates of silver nitrate. It was therefore felt that the desired quaternary ammonium salt in varying stages of purity was in hand and that one preparation should be selected for bioassay. The preparation melting at 189.9–190.6° (darkens) cor. was available in some quantity, and this was chosen for bioassay and inclusion in Table I.

Oximes.—Samples of all the bromides in the β-naphthacyl series were warmed on the steam-bath for several hours in aqueous solution with a 15% excess of hydroxylamine hydrochloride and sodium acetate. In many instances there was evidence of decomposition of the bromide, but in several cases, pure oximes could be isolated. These are listed in Table II.

NATIONAL CANCER INSTITUTE
NATIONAL INSTITUTE OF HEALTH
U. S. PUBLIC HEALTH SERVICE
BETHESDA, MARYLAND

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A Crystal-Chemical Study of Cesium Trichlorocuprate[1]

BY HAROLD P. KLUG[2] AND GEORGE W. SEARS, JR.[3]

During the investigation of the nature of inorganic halogen complexes with certain elements, the compound cesium trichlorocuprate, $CsCuCl_3$, was studied. It was hoped that from its study information concerning the coördination of chlorine around copper, and the nature of the groups present in the crystalline trichlorocuprates might be obtained. Although such complete results have not been achieved, certain data were obtained which are reported in this communication.

The salt was prepared by the evaporation, over anhydrous calcium chloride, of a solution of the constituent salts containing cupric chloride in considerable excess, as described by Wells and Dupre.[4]

Gravimetric analysis for copper and chlorine confirmed the identity and composition of the garnet-red crystals.

Anal. Calcd. for $CsCuCl_3$: Cu, 20.99; Cl, 35.12. Found: Cu, 20.68; Cl, 34.77.

Since no crystallographic data were available, other than the observation of Wells and Dupre[4] that the crystals formed slender hexagonal prisms, a goniometric study was made.[5]

The chief habit proved to be the slender needles exhibiting the first-order hexagonal prism and terminated by one or more first-order pyramids. A few crystals of a different habit were observed, however, in which the first-order prism was missing, or nearly so, and one of the pyramids ($10\bar{1}3$), predominated. The average results of the measurements on six crystals are given in Table I in terms of the new notation for the hexagonal system as described by Palache, Berman and Frondel.[6] The data of Table I lead to the axial ratio, $c = 2.522$.

TABLE I

ANGULAR DATA ON CESIUM TRICHLOROCUPRATE

Form		ϕ	ρ
c	0001	....	0° 00′
m	$10\bar{1}0$	30° 00′	90 00
r	$10\bar{1}1$	30 00	71 03
n	$10\bar{1}2$	30 00	55 32
l	$10\bar{1}3$	30 00	44 08

The crystals show parallel extinction between crossed nicols. Pleochroism is strong, the color changing from a canary yellow to an orange brown in thin sections. Absorption is strongest when the direction of elongation is perpendicular to the plane of polarization. There was no evidence of twinning in the crystals examined by polarized light or on the goniometer. A good cleavage perpendicular to the needle axis was observed. Unusually detailed pyroelectric experiments by the method of Martin[7] and also that of Orelkin and Lonsdale[8] failed to give a positive test along either the vertical axis or the horizontal axes. The average value of the density from three pycnometric determinations at 24° was 3.644. The crystallographic study thus indicates the crystal symmetry class to be the normal or holohedral class of the hexagonal system, D_6^h.

Laue, rotating and oscillating crystal photographs, and *c* axis Weissenberg patterns were used in the X-ray study of the crystals. The dimensions of the unit cell were found to be $a_0 = 7.175 \pm 0.002$Å. and $c_0 = 18.03 \pm 0.03$Å. These lead to the axial ratio $c = 2.513$, in satisfactory agreement with the value from the goniometric study. The X-ray data indicated no absent types of reflections whatsoever in the first order. The lattice is therefore primitive, and the space group is either D_{6h}^1, D_6^1, C_{6v}^1, D_{3h}^1, or D_{3h}^3. Since there is no evidence for the lack of a center of symmetry the correct space group appears to be D_{6h}^1–$C6/mmm$. The unit cell contains 6 $CsCuCl_3$.

Much detailed study by the Patterson–Harker Fourier technique and other methods has failed to yield an atomic arrangement for the crystal in satisfactory agreement with the X-ray intensity data. From the dimensions of the cell it is hard to escape the conclusion that the structure is based on a close-packed arrangement of cesium and chloride ions, as in the case of $Cs_3As_2Cl_9$ and $Cs_3Tl_2Cl_9$.[9] No reasonable packing of the Cs^+ and

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(1) From a thesis by George W. Sears, Jr., presented to the Graduate Faculty of the University of Minnesota in partial fulfillment of the requirements for the Ph.D. degree, January, 1944.

(2) Present address: Mellon Institute, Pittsburgh 13, Pa.

(3) Present address: E. I. du Pont de Nemours & Company, Wilmington, Delaware.

(4) Wells and Dupre, *Am. J. Sci.*, [3] **47**, 94 (1894).

(5) The authors wish to express their thanks to Professor John W. Gruner of the Department of Mineralogy for his valuable assistance in connection with the goniometric measurements and the microscopic observations.

(6) Palache, Berman and Frondel, "Dana's System of Mineralogy," 7th ed., Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1944, pp. 9, 23–31.

(7) Martin, *Min. Mag.*, **22**, 519 (1931).

(8) Orelkin and Lonsdale, *Proc. Roy. Soc.* (London), **A144**, 633 (1934).

(9) Hoard and Goldstein, *J. Chem. Phys.*, **3**, 117 and 199 (1935).