

of nascent bromine. After refluxing until all free bromine was expelled the insoluble reaction product was separated and recrystallized from hot water. It melted with decomposition at 260–261° and was identified as 6-methyl-5-bromouracil. The yield was quantitative.

*Anal.* Calcd. for  $C_5H_6O_2N_2Br$ : C, 29.26; H, 2.63; N, 13.65. Found: C, 29.26; H, 2.43; N, 13.88.

This same decomposition was accomplished by boiling a solution of the pyrimidine II in acetic anhydride. The yield was quantitative.

#### Behavior of the Ether VII on Reduction

1. **Action of Tin Chloride and Hydrochloric Acid.**—One half a gram of the bicyclouracil compound VII was digested at 100° in 15 cc. of dilute hydrochloric acid with 2 g. of stannous chloride for six hours. The mixture was then allowed to cool when colorless crystalline material deposited. This was identified as a mixture of 6-methyl-5-chlorouracil and the unreduced bicyclo compound VII. The difference in water solubility permitted easy separation and the 6-methyl-5-chlorouracil was obtained in the form of prisms which did not melt below 300°. The recovered bicyclo compound VII crystallized from boiling water and melted at 270–275° with decomposition.

*Anal.* Calcd. for  $C_{10}H_8O_5N_4Cl_2$ : N, 16.71. Found: N, 16.74, 16.69.

2. **Action of Hydriodic Acid.**—One gram of the bicyclo compound VII, melting at 270–275° was boiled for fifteen minutes with 10 cc. of hydriodic acid of sp. gr. 1.5 and an excess of red phosphorus. The resulting solution was then diluted with 30 cc. of water and filtered while hot. A colorless solution resulted which deposited a small amount of crystals that were filtered off and identified as 6-methyl-5-chlorouracil. The acid filtrate was concentrated by evapo-

ration at 100° to a small volume and cooled when 6-methyluracil I separated. This was purified by crystallization from hot water and did not melt below 300°. It was free from chlorine.

*Anal.* Calcd. for  $C_5H_6O_2N_2$ : C, 47.63; H, 4.76; N, 22.22. Found: C, 47.62; H, 4.66; N, 22.33.

**Action of Ammonia on 6-Methyl-5-dichloroxyhydrouracil III.**—Two grams of this pyrimidine was dissolved in 50 cc. of concentrated aqueous ammonia and the solution preserved at ordinary temperature in a stoppered bottle. After standing one week the solution was evaporated at 100° to expel the excess of ammonia and the filtrate cooled. Pure 6-methyl-5-chlorouracil separated and was the only product identified, and did not melt below 300°. We obtained no evidence of the formation of the bicyclo compound VII.

#### Summary

1. 6-Methyl-5,5-dichloroxyhydrouracil III is converted by the action of hydrochloric acid into a dichloro ether derivative of the hypothetical 6-methyl-6-oxy-1,5-bicyclouracil VII.

2. The corresponding 6-methyl-5,5-dibromoxyhydrouracil II is transformed by action of hydrochloric acid into 6-methyl-5-bromouracil. No evidence of the formation of a bicyclouracil derivative was obtained.

3. These same respective changes can also be brought about by the action of acetic anhydride.

NEW HAVEN, CONNECTICUT RECEIVED MARCH 11, 1943

[CONTRIBUTION FROM RESEARCH LABORATORIES OF NOCOCOL CHEMICAL MFG. CO., INC.]

## Preparation of Aminobenzoic Acid Esters of Substituted Monoalkyl Amino Alcohols. II

BY WILLIAM F. RINGK<sup>1</sup> AND ELIAS EPSTEIN

In a previous paper,<sup>1a</sup> the author described the amino benzoates of  $\beta$ -alkylamino- $\alpha,\alpha$ -dimethylethanol where the alkyl group contained from 1 to 5 carbon atoms.

This paper deals with members of the same series in which the nitrogen alkyl group contains 6 to 8 carbon atoms which were made for comparison with members of another series.

In general, the amino alcohols were prepared as previously described, with the following exceptions: the solvent used was 50% isopropanol solution and the mixtures were refluxed for about sixty hours. The yields were approximately 45%.

(1) Present address: Benzol Products Company, Newark, N. J.

(1a) Goldberg, Ringk and Spoerri, *THIS JOURNAL*, **61**, 3562 (1939).

Table I gives the physical constants of the amino alcohols and the molecular refractions.

The amino alcohols were condensed with *p*-nitrobenzoyl chloride in an aqueous alkaline medium as described in our previous paper. The nitro esters are all yellow solids which give positive nitroso tests.

TABLE Ia  
 $\beta$ -ALKYLAMINO- $\alpha,\alpha$ -DIMETHYLETHANOLS  
[ $RNHCH_2C(CH_3)_2OH$ ]

Alkyl group	B. p., °C.	$d_{20}^{20}$	$n_D^{20}$	MR, calcd.	MR, found	Diff.
<i>n</i> -Hexyl	224–228	0.8618	1.4406	53.35	53.05	–0.30
<i>n</i> -Heptyl	242–246	.8567	1.4424	57.95	57.85	–.10
Octyl-2	245–248	.8560	1.4410	61.56	62.09	–.53
2-Ethylhexyl	245–248	.8560	1.4436	61.56	62.42	–.86

TABLE Ib  
 $\beta$ -MONOALKYLAMINO- $\beta,\beta$ -DIMETHYLETHANOLS  
 $[\text{RHNC}(\text{CH}_3)_2\text{CH}_2\text{OH}]$

$\beta$ -Mono alkyl group	Empirical formula	B. p., °C.	M. p., °C.
Ethyl <sup>a,b</sup>	$\text{C}_8\text{H}_{15}\text{ON}$	167-169	72-73
<i>n</i> -Propyl <sup>a,b</sup>	$\text{C}_7\text{H}_{17}\text{ON}$	183-186	55-57
<i>i</i> -Propyl <sup>a</sup>	$\text{C}_7\text{H}_{17}\text{ON}$	172-175	40-42
<i>n</i> -Butyl <sup>a,b</sup>	$\text{C}_8\text{H}_{19}\text{ON}$	200-203	68-69
<i>i</i> -Butyl <sup>a,b</sup>	$\text{C}_8\text{H}_{19}\text{ON}$	192-194	45-46
<i>s</i> -Butyl	$\text{C}_8\text{H}_{19}\text{ON}$	186-190	Liquid
<i>n</i> -Amyl <sup>a,b</sup>	$\text{C}_9\text{H}_{21}\text{ON}$	223-230	59-60
<i>i</i> -Amyl <sup>a,b</sup>	$\text{C}_9\text{H}_{21}\text{ON}$	211-215	73-74
<i>n</i> -Hexyl <sup>b</sup>	$\text{C}_{10}\text{H}_{23}\text{ON}$	235-238	62-63
Ethylbutyl	$\text{C}_{10}\text{H}_{23}\text{ON}$	220-226	Liquid
<i>n</i> -Heptyl <sup>b</sup>	$\text{C}_{11}\text{H}_{25}\text{ON}$	253-258	50-52
(Octyl-2)	$\text{C}_{12}\text{H}_{27}\text{ON}$	250-255	Liquid
2-Ethylhexyl	$\text{C}_{12}\text{H}_{27}\text{ON}$	249-255	15-17
<i>n</i> -Decyl	$\text{C}_{14}\text{H}_{31}\text{ON}$	295-300	55-57

<sup>a</sup> Also prepared by Kremer and Waldman.<sup>2</sup> <sup>b</sup> Also prepared by Pierce, Salisbury, Haden and Willis.<sup>3</sup>

The hydrochlorides were all viscous yellow oils while the sulfates were white crystalline solids. In Table II are summarized the physical constants of the amino ester sulfates and their analyses.

The other series of amino alcohols referred to above, namely, the  $\beta$ -alkylamino- $\beta,\beta$ -dimethylethanol (2 - alkylamino - 2 - methyl - 1 - propanols) have been reported in THIS JOURNAL by Kremer and Waldman<sup>2</sup> and by J. S. Pierce, Salisbury, Haden and Willis.<sup>3</sup> Pierce and his co-workers reported the alkoxybenzoates, while Kremer and Waldman reported the *p*-nitrobenzoates.

The latter men reported poor yields and non-reproducible results when using the condensation procedure originally outlined by Goldberg and Whitmore.<sup>4</sup> On repeating their condensation procedure, using pyridine as a solvent, we ob-

TABLE IIa  
 $\beta$ -MONOALKYLAMINO- $\alpha,\alpha$ -DIMETHYLETHYL *p*-AMINO BENZOATE SULFATES  $[\text{RNHCH}_2\text{C}(\text{CH}_3)_2\text{OOCOC}_6\text{H}_4\text{NH}_2]_2\cdot\text{H}_2\text{SO}_4$

Alkyl group	Mol. wt.	M. p., °C.	Empirical formula	Calcd. % C	Found	Calcd. % H	Found	Calcd. % N	Found
<i>n</i> -Hexyl	682.91	169-171	$\text{C}_{34}\text{H}_{58}\text{O}_8\text{N}_4\text{S}$	59.79	59.59	8.56	8.43	8.21	7.98
<i>n</i> -Heptyl	710.95	169-172	$\text{C}_{36}\text{H}_{62}\text{O}_8\text{N}_4\text{S}$	60.80	60.65	8.79	8.56	7.88	7.60
Octyl-2- $\frac{1}{2}\text{H}_2\text{O}$	748.01	154-156	$\text{C}_{38}\text{H}_{66}\text{O}_8\text{N}_4\text{S}$	60.29	60.57	9.05	9.14	7.40	7.45
2-Ethylhexyl	739.00	141-143	$\text{C}_{38}\text{H}_{66}\text{O}_8\text{N}_4\text{S}$	61.76	61.66	9.00	9.11	7.53	7.41

TABLE IIb  
 $\beta$ -MONOALKYLAMINO- $\beta,\beta$ -DIMETHYLETHYL *p*-AMINO BENZOATE HYDROCHLORIDES  $[\text{RNHC}(\text{CH}_3)_2\text{CH}_2\text{OOCOC}_6\text{H}_4\text{NH}_2\cdot\text{HCl}]$

$\beta$ -Mono alkyl group	Mol. wt.	M. p., °C.	Empirical formula	Calcd. % C	Found	Calcd. % H	Found	Calcd. % N	Found
Ethyl	272.77	245-246.5	$\text{C}_{13}\text{H}_{21}\text{O}_2\text{N}_2\text{Cl}$	57.24	57.26	7.76	8.03	10.27	10.46
<i>n</i> -Propyl	286.80	239-240	$\text{C}_{14}\text{H}_{23}\text{O}_2\text{N}_2\text{Cl}$	58.63	58.60	8.08	8.01	9.77	9.94
<i>i</i> -Propyl	286.80	234.5-236	$\text{C}_{14}\text{H}_{23}\text{O}_2\text{N}_2\text{Cl}$	58.63	58.42	8.08	7.94	9.77	...
<i>n</i> -Butyl	300.83	192-192.5	$\text{C}_{15}\text{H}_{25}\text{O}_2\text{N}_2\text{Cl}$	59.89	59.78	8.38	8.13	9.31	9.45
<i>i</i> -Butyl	300.83	225.8-228	$\text{C}_{15}\text{H}_{25}\text{O}_2\text{N}_2\text{Cl}$	59.89	59.95	8.38	8.40	9.31	9.41
<i>s</i> -Butyl-1 $\text{H}_2\text{O}$	318.85	202-205	$\text{C}_{15}\text{H}_{27}\text{O}_2\text{N}_2\text{Cl}$	56.50	56.73	8.65	8.46	8.79	8.62
<i>n</i> -Amyl	314.85	209-211.8	$\text{C}_{16}\text{H}_{27}\text{O}_2\text{N}_2\text{Cl}$	61.04	60.93	8.65	8.40	8.90	9.05
<i>i</i> -Amyl	314.85	202-203	$\text{C}_{16}\text{H}_{27}\text{O}_2\text{N}_2\text{Cl}$	61.04	60.82	8.65	8.84	8.90	9.13
<i>n</i> -Hexyl	328.88	212.5-213.5	$\text{C}_{17}\text{H}_{29}\text{O}_2\text{N}_2\text{Cl}$	62.08	62.26	8.90	8.95	8.52	8.49
Ethylbutyl	328.88	198-199.5	$\text{C}_{17}\text{H}_{29}\text{O}_2\text{N}_2\text{Cl}$	62.08	62.29	8.90	8.73	8.52	8.50
<i>n</i> -Heptyl	342.90	197-198	$\text{C}_{18}\text{H}_{31}\text{O}_2\text{N}_2\text{Cl}$	63.04	62.95	9.11	9.05	8.17	8.22
Octyl-2- $\frac{1}{2}\text{H}_2\text{O}$	365.93	137-140	$\text{C}_{19}\text{H}_{33}\text{O}_2\text{N}_2\text{Cl}$	62.36	62.66	9.37	9.52	7.66	7.40
2-Ethylhexyl	356.93	154-158	$\text{C}_{19}\text{H}_{33}\text{O}_2\text{N}_2\text{Cl}$	63.93	63.88	9.05	9.42	7.85	8.04
<i>n</i> -Decyl	384.98	141-142	$\text{C}_{20}\text{H}_{35}\text{O}_2\text{N}_2\text{Cl}$	65.51	65.23	9.69	9.90	7.28	7.16

TABLE IIc  
 $\beta$ -MONOALKYLAMINO- $\beta,\beta$ -DIMETHYLETHYL *m*-AMINO BENZOATES

$\beta$ -Mono alkyl group	Mol. wt.	M. p., °C.	Empirical formula	Calcd. % C	Found	Calcd. % N	Found
Ethyl (sulfate)	570.68	223-224	$\text{C}_{26}\text{H}_{42}\text{O}_8\text{N}_2\text{S}$	54.72	54.59	7.42	7.21
<i>n</i> -Propyl (hydrochloride)	286.80	192-194	$\text{C}_{14}\text{H}_{23}\text{O}_2\text{N}_2\text{Cl}$	58.63	...	8.08	...
<i>i</i> -Propyl (sulfate)	598.74	188-189	$\text{C}_{26}\text{H}_{46}\text{O}_8\text{N}_2\text{S}$	56.16	...	7.75	...
<i>n</i> -Butyl (hydrochloride)	300.83	205-208	$\text{C}_{15}\text{H}_{25}\text{O}_2\text{N}_2\text{Cl}$	59.89	59.71	8.38	8.52
<i>i</i> -Butyl (hydrochloride)	300.83	oil	$\text{C}_{15}\text{H}_{25}\text{O}_2\text{N}_2\text{Cl}$	59.89	...	8.38	...
<i>i</i> -Butyl (sulfate)	626.80	oil	$\text{C}_{30}\text{H}_{50}\text{O}_8\text{N}_2\text{S}$	57.48	...	8.04	...

The nitro esters were reduced with iron and hydrochloric acid to the anesthetic amino esters.

(2) Kremer and Waldman, THIS JOURNAL, **64**, 1089 (1942).

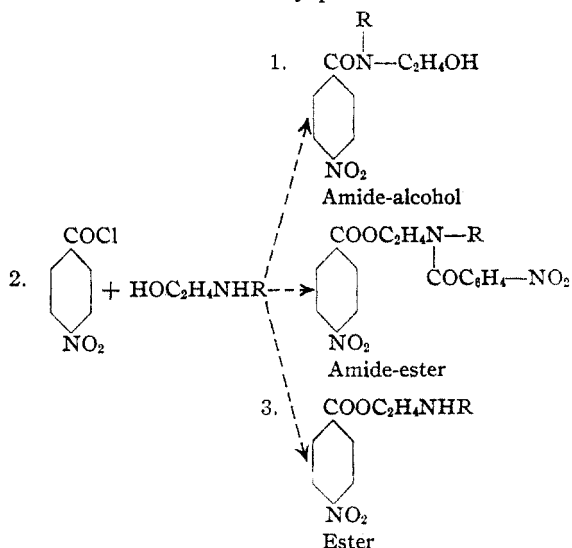
(3) Pierce, Salisbury, Haden and Willis, *ibid.*, **64**, 2884 (1942).

(4) S. D. Goldberg and W. F. Whitmore, *ibid.*, **59**, 2280 (1937).

tained what we believe is a solid isomeric amide-alcohol, rather than a viscous, yellow oily *p*-nitrobenzoate which we had previously obtained by our method of condensation. The melting point of this amide checked with the compound they report as the *p*-nitrobenzoate.

We offer the following as evidence that amide rather than ester formation takes place when pyridine is used as a solvent.

Goldberg<sup>5</sup> in his doctoral dissertation points out that the condensation may proceed as follows



This is logical in view of the fact that the amino alcohols contain two reactive hydrogen atoms.

Since we usually reduce the nitro esters immediately, we repeated our work on the *n*-butyl nitrobenzoate and isolated it as a viscous, yellow oil. On allowing this to stand for several weeks, the material started to crystallize. After several recrystallizations from ethanol it melted at 195–196°, which coincided with the value given by Kremer and Waldman. A mixed melting point of this material and the compound we made in accordance with their procedure showed no depression. On reduction, neither compound yields a product which is anesthetic to the tongue whereas our liquid nitrobenzoate yields a powerful anesthetic base.

The molecular rearrangement of the nitrobenzoate to the amide-alcohol which occurred on standing, was surprising to us in view of the fact that the ester was pure, contained no solvent and stood at room temperature. Reasenberg,<sup>6</sup>

(5) S. D. Goldberg, Doctoral Dissertation, Polytechnic Institute of Brooklyn, June, 1935, p. 35.

(6) J. R. Reasenberg, Doctoral Dissertation, Polytechnic Institute of Brooklyn, June, 1941, pp. 14–25.

however, made a thorough search of the literature on this subject and cites numerous examples of this shift which, while not well known, is quite often referred to.

To summarize the remainder of our findings, we found the amide to be insoluble in ether, the nitro ester, very soluble; the amide soluble in hot water, the ester, insoluble; the ester giving a positive nitroso test for secondary amines, the amide, negative; the amide insoluble in cold, concentrated hydrochloric acid, the ester completely soluble. No attempt has been made by us to give a rigid proof of structure of the amide-alcohol since we do not have sufficient time available for this work.

Using 2-amino-2-methyl-1-propanol and an excess of halide with isopropanol as a solvent and refluxing for from eight to twenty-four hours, the 2-alkylamino-2-methyl-1-propanols were prepared. They were isolated by adding hydrochloric acid to the reaction mixture and vacuum distilling to a sirup. An excess of a 30% sodium hydroxide solution was added, with cooling, to the residue in the flask and an ether extract made of the amino alcohol. The ether was evaporated and the residue vacuum distilled. The pure amino alcohol was obtained by careful fractionation. In preparing some of the higher members of the series it was found advisable to use an excess of the primary amino alcohol in order to obtain better yields. The yields varied from 20 to 60%.

The amino alcohols were condensed with *p*-nitrobenzoyl chloride in an aqueous alkaline solution keeping the temperature between 30–40°, with vigorous stirring. The nitrobenzoates were extracted with ether and the ether evaporated.

The nitro esters were immediately reduced with iron and hydrochloric acid and the free base converted to the salt by an appropriate acid.

### Experimental

The preparation of  $\beta$ -*n*-propyl-amino- $\beta$ , $\beta$ -dimethylethanol and the condensation with *p*-nitrobenzoyl chloride is described below.

**$\beta$ -*n*-Propylamino- $\beta$ , $\beta$ -dimethylethanol** ( $n$ -C<sub>3</sub>H<sub>7</sub>NHC-(CH<sub>3</sub>)<sub>2</sub>CH<sub>2</sub>OH).—To 178 g. (2.0 moles) of 2-amino-2-methyl-1-propanol contained in a flask was added 492 g. (4.0 moles) of *n*-propyl bromide and 900 g. of isopropanol and the mixture refluxed for sixteen hours; 50 cc. of concentrated hydrochloric acid was added to the cooled reaction mixture which was then vacuum distilled to a sirupy mass. An excess of a 30% sodium hydroxide solution was added to the residue causing an oil to separate which was then extracted with ether. The ether was removed by

TABLE III  
(a)  $\beta$ -MONOALKYLAMINO- $\beta,\beta$ -DIMETHYLETHYL *p*-AMINO BENZOATE HYDROCHLORIDES  
[RNHC(CH<sub>3</sub>)<sub>2</sub>CH<sub>2</sub>OCC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>·HCl]

$\beta$ -Mono alkyl group	Toxicity		Relative toxicity (sub.) based on M. L. D. of procaine	Relative potency		Anesthetic efficiency	
	Intra- peritoneal, M. L. D. mg./kg.	Subcu- taneous M. L. D. mg./kg.		Surface based on cocaine	Conductive based on procaine	Surface based on cocaine	Conductive based on procaine
Ethyl	220	300	2.5	1	4	2.0	1.6
<i>n</i> -Propyl	130	..	..	3	4	..	..
<i>i</i> -Propyl	190	250	3.0	2	4	3.3	1.8
<i>n</i> -Butyl	70	..	..	3	8	..	..
<i>i</i> -Butyl	80	120	6.2	2	4	1.6	0.7
<i>s</i> -Butyl	...	90	8.3	1.5	..	0.9	..
<i>n</i> -Amyl	50	..	..	6	..	..	..
<i>i</i> -Amyl	70	..	..	4	5	..	..
<i>n</i> -Hexyl	60	..	..	5	..	..	..
Ethylbutyl	...	40	19	5	..	1.3	..
<i>n</i> -Heptyl	60	..	..	15	..	..	..
Octyl-2	90	240	3.1	15	25	24	8.1
2-Ethylhexyl	60	60	12.5	15	20	6	1.6
<i>n</i> -Decyl	60	..	..	15	20	..	..

(b)  $\beta$ -Monoalkylamino- $\beta,\beta$ -dimethylethyl *m*-aminobenzoate salts

Ethyl (sulfate)	...	2500	0.3	0.5	4	8.5	13
<i>i</i> -Propyl (sulfate)	...	900	0.8	1	4	6.5	5
<i>n</i> -Propyl (hydrochloride)	...	850	0.9	1.5	8	8.3	9
<i>n</i> -Butyl (hydrochloride)	190	310	2.4	2	4	4.2	1.7

(c) Standard anesthetics

Procaine	250	750	1	..	1	..	1
Monocaine	250	450	1.6	..	4	..	2.5
Cocaine	...	150	5	1	..	1	..
Butyn	...	80	9.4	1.5	..	0.8	..

distillation and the residue vacuum distilled. The fraction boiling at 56–66° at 3 mm. pressure was fractionated at atmospheric pressure and boiled at 183–186°. The yield was 57%. The amino alcohol melts at 55.0–57.0° and gives a positive nitroso test. Table Ib lists the physical constants of the other members of this series.

*beta-n*-Propyl-amino-*beta*,*beta*-dimethylethyl-*p*-amino-benzoate ( $n$ -C<sub>3</sub>H<sub>7</sub>NHC(CH<sub>3</sub>)<sub>2</sub>CH<sub>2</sub>OCC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>).—Certain refinements have been made in this condensation method since publication of our last paper.<sup>1</sup>

Sixteen grams of sodium hydroxide was dissolved in 1200 cc. of water contained in a beaker and 50 g. of  $\beta$ -*n*-propyl-amino- $\beta,\beta$ -dimethylethanol added and the mixture stirred vigorously. Seventy-two grams of *p*-nitrobenzoyl chloride was dissolved in ether and this solution added gradually with vigorous stirring, maintaining the temperature between 35–40°. The addition usually takes about one-half hour and the stirring is continued for an additional half hour. The reaction mixture is transferred to a separatory funnel and additional ether added. The ether extract is washed several times with water and then dried over anhydrous sodium sulfate. The ether is then evaporated and the nitro ester immediately reduced by means of iron and hydrochloric acid. The purified amino ester is then treated with the calculated quantity of hydrochloric acid to form the mono hydrochloride of the amino ester. Table IIb lists the constants of the *p*-aminobenzoate hydrochlorides and Table IIc the constants of the *m*-aminobenzoate salts.

The  $\beta$ -*n*-butylamino- $\beta,\beta$ -dimethylethyl-*o*-aminobenzoate was prepared. On sublimation this compound melts at 68–69°. The hydrochloride, sulfate and phosphate were liquids.

### Pharmacology

A preliminary pharmacological investigation of the  $\beta,\beta$ -dimethyl series of compounds shows them to be very potent anesthetics and, in general, less toxic than the corresponding members of the  $\alpha,\alpha$ -dimethyl series.

In Table IIIa, b and c we have summarized the results of our work on intraperitoneal and subcutaneous toxicity, relative subcutaneous toxicity, surface and conductive potency, surface anesthetic efficiency (ratio of surface potency to relative subcutaneous toxicity) and conductive anesthetic efficiency (ratio of conductive potency to relative subcutaneous toxicity). Intraperitoneal and subcutaneous toxicity was determined in the white male mouse weighing between 18–25 g. Surface anesthetic potency was determined on the rabbit cornea by the method outlined by Abramson and Goldberg.<sup>7</sup> Conductive anesthetic potency was

(7) Abramson and Goldberg, *J. Pharmacol.*, **62**, 69 (1938).

done on the sciatic nerve of the intact guinea pig according to the method of Shackell.<sup>8</sup>

An insufficient number of animals was used to determine accurately the subcutaneous toxicity in the guinea pig and the intravenous toxicity in the rabbit.

The members of this series of anesthetics appear to be vaso-dilators as determined by intravenous injection in the cat. However, they act synergistically with epinephrine. The relative conductive potency figures shown in Table III are based upon the use of solutions containing various concentrations of each anesthetic, with epinephrine 1:60,000.

The outstanding member of this series of anesthetics is the octyl-2 derivative which we call Octacaine. An examination of Table III shows that octacaine has the highest anesthetic effi-

ciency ratio for surface anesthesia, being 24 times as efficient as cocaine. It is 8 times more efficient as a conductive anesthetic than procaine. The *m*-amino derivatives are considerably less toxic than the corresponding *p*-amino compounds.

Dr. Frank Co Tui, of the New York University School of Medicine, will shortly publish a complete pharmacological report on Octacaine.

### Summary

1. Four new members of a series of previously reported  $\beta$ -alkylamino- $\alpha,\alpha$ -dimethylethanols and the salts of the *p*-aminobenzoates are described.

2. A series of  $\beta$ -alkylamino- $\beta,\beta$ -dimethylethanols and the salts of the aminobenzoates are also described.

3. A preliminary pharmacological investigation of these anesthetics is reported.

BROOKLYN, NEW YORK

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(8) Shackell, *Anesthesia and Analgesia*, **14**, 20 (1935).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

## The Thermal Diagram of the System Iron-Tin<sup>1,2</sup>

BY W. F. EHRET AND D. H. GURINSKY<sup>3</sup>

Equilibria in the iron-tin system have been studied rather extensively during the last two decades.<sup>4</sup> Wever and Reinecken,<sup>5</sup> using thermal, magnetometric and microscopic methods, concluded that the system possessed two intermetallic compounds, Fe<sub>3</sub>Sn and FeSn<sub>2</sub>. Preece and Edwards,<sup>6</sup> using similar methods, reported three compounds: Fe<sub>3</sub>Sn, FeSn and FeSn<sub>2</sub>. The X-ray work of Ehret and Westgren<sup>7</sup> confirmed the three compounds just mentioned but these investigators found two additional phases, a high temperature modification of FeSn, which they called  $\gamma$  (NiAs structure), and a  $\beta'$  phase at approximately 60% Sn, which corresponds to Fe<sub>3</sub>Sn<sub>2</sub>. They were not certain whether the latter really was a single phase or a mixture of two. Its lower

limit of stability lay between 550 and 600°. In the most recent work on this system, that by Jones and Hoare,<sup>8</sup> alloy samples were heat treated and then examined microscopically. These investigators were able to substantiate the phase diagram of Preece and Edwards, and concluded that the  $\gamma$  phase of Ehret and Westgren did not exist at 68.5% Sn and 850°.

Because of the differences in the conclusions drawn in the above-mentioned reports, the present authors undertook the reexamination of this system with the view of clarifying the situation so far as it concerned equilibria existing above 500° and in the range of 10 to 100% Sn. It was felt that below 500° the diagram had been correctly established.

### Experimental

The rather well-known techniques of heat treating, quenching, and X-ray analysis were employed as the chief means of investigation. Microscopic examination served as an auxiliary means. The alloys were prepared from Wemco research iron<sup>9</sup> and redistilled tin<sup>10</sup> melted together in magnesia crucibles. Most of the melts were made in a

(1) Presented before the Division of Physical and Inorganic Chemistry at the Buffalo meeting, September 9, 1942.

(2) Condensed from the doctoral dissertation of D. H. Gurinsky, October, 1942.

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(4) For a review of all work published to date on the iron-tin system, including practical aspects, the reader is referred to an article on "The Constitution of the Iron-Tin Alloys" by O. E. Romig which appeared in *Metal Progress*, **42**, 899 (1942).

(5) Wever and Reinecken, *Z. anorg. allgem. Chem.*, **151**, 349 (1926).

(6) Preece and Edwards, *J. Iron Steel Inst. (London)*, **124**, 41 (1931).

(7) Ehret and Westgren, *THIS JOURNAL*, **55**, 1339 (1933).

(8) Jones and Hoare, *J. Iron Steel Inst. (London)*, **129**, 273 (1934).

(9) Westinghouse Electric and Supply Co., East Pittsburgh, Penna.

(10) Vulcan Detinning Works, Sewaren, N. J.