filtration and washed with ether to give after drying 0.42 g. (3.5%) of white needles, m.p. 182–186° dec.

The crude product was benzenesulfonated without further purification.

4-Benzenesulfonamido-3-hydroxytriphenylmethane.—To 0.42 g. of 4-amino-3-hydroxytriphenylmethane sulfate in 10 ml. of dry pyridine was added 0.25 g. of benzenesulfonyl chloride. The mixture was heated under reflux for 3 minutes and allowed to cool to room temperature spontaneously. After 30 hours the reaction mixture was poured into 20 ml. of 1:1 hydrochloric acid (ice) to give a dark oil which solidified on standing several hours. The yield of tan product was 0.45 g. (83.5%). Three recrystallizations from ethanol–water (Darco) gave white micro-needles, m.p. 147–148° with some previous sintering at 146°.

Anal. Calcd. for $C_{25}H_{21}NO_3S$: C, 72.26; H, 5.10; N, 3.37. Found: C, 72.27; H, 5.06; N, 3.16.

Infrared analysis indicated NH bands at 3260 (stretch) and 1524 cm.$^{-1}$ (bend); C–N (stretch) band at 1235 cm.$^{-1}$; an OH band at 3400 cm.$^{-1}$; C–O (stretch) bands at 1343 and 1235 cm.$^{-1}$; SO_2 bands at 1322 and 1162 cm.$^{-1}$; monosubstituted benzene bands at 752, 724, 700 and 679 cm.$^{-1}$.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE MORLEY CHEMICAL LABORATORY, WESTERN RESERVE UNIVERSITY]

Mercuration of Certain Aromatic Compounds[1,2]

BY GEORGE R. JACKSON, JR.[3] AND MARTIN S. FRANT[4]

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A quantitative investigation of the classical mercuration of *p*-toluidine, benzoic acid, nitrobenzene, and benzenesulfonic acid is reported. The mercury compounds were converted to the corresponding bromine derivatives and determined cryoscopically for *p*-toluidine, by infrared spectroscopy for the latter three compounds. The mercuration of *p*-toluidine goes almost exclusively *ortho* to the amino group; benzoic acid averaged *o:m:p* 57:25:18. The *meta* and *para* isomers have not been reported previously. The results of the mercuration of nitrobenzene agree substantially with those in the literature, *o:m:p* 53:32:15. Both the *ortho* and *para* isomers were found from the mercuration of benzenesulfonic acid, as well as the previously reported meta derivative, the approximate ratio being *o:m:p* 24:61:15.

Aromatic mercuration has been reported by many investigators as giving anomalous orientation effects.[5] Thus, mercuration of benzoic acid was reported to give the *ortho* product exclusively,[6] nitrobenzene principally *ortho* and *para*,[7,8] toluene substantial quantities of the *meta* isomer,[9] while phenol was reported as mercurating only in the *ortho* and *para* positions.[10–12] A report on the mercuration of benzenesulfonic acid indicates that the mercury enters the nucleus in the position *meta* to the sulfonic acid group.[13]

The development of a workable hypothesis for the mechanism of mercuration by the classical method (with mercuric acetate in non-polar solvents) has been handicapped by the lack of quantitative data on the relative amounts of the possible isomers obtained. The chief experimental problem in such work is the difficulty of quantitatively separating the isomers obtained. This has often meant that when but one isomer was reported, others may have been present, but not isolated.

The present work deals with an investigation of the classical mercuration of *p*-toluidine, benzoic acid, nitrobenzene and benzensulfonic acid. In each case the mercury compounds were converted to the corresponding bromine derivatives, and compared with known bromine derivatives.[14]

The possible bromo isomers in the case of *p*-toluidine were determined cryoscopically, and in the other three instances by infrared spectroscopy. The advantage of this method over previous procedures is that it is not necessary to isolate and purify each of the isomeric products, and greatly reduces the possibility of errors in the actual ratio of isomers.

The purpose of this paper is to provide quantitative data for the study of the mechanism of aromatic mercuration.

Experimental

Materials. Mercuric Acetate.—The mercuric acetate used throughout this investigation was Mallinckrodt analytical reagent grade. ***p*-Toluidine**: Eastman Kodak white label product was recrystallized from 20% ethanol-water solution, and then vacuum distilled. **3-Bromo-4-acetylaminotoluene**: The 3-bromo-4-acetylaminotoluene as well as the corresponding amino compound were obtained from Eastman Kodak Co. The amide was recrystallized to constant melting point (see Table I).

2-Bromo-4-acetylaminotoluene.—The 2-bromo-4-nitrotoluene was prepared by the bromination of *p*-nitrotoluene according to the method of Lucas and Scudder,[15] and melted at 76.5–78.0° (lit. 78°). The reduction of the nitro group was effected by use of a 50% alcohol solution of ammonium sulfide, and the resulting amine dissolved in ether and dried. The ether solution was treated with dry hydrogen chloride gas and a yellow amine salt precipitated out. This was converted to the amide by acetic anhydride, and recrystallized from methanol.

***o*-, *m*- and *p*-Bromobenzoic Acids.**—Eastman Kodak Co. *o*-, *m*- and *p*-bromobenzoic acids were recrystallized twice from methanol.

***o*-, *m*- and *p*-Bromonitrobenzene.**—Eastman Kodak Co. *o*- and *p*-bromonitrobenzene were recrystallized twice from ethanol, using Nuchar in the first recrystallization. *m*-

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[1] Presented at the 124th National Meeting of the American Chemical Society, Chicago, Ill., September 10, 1953.

[2] From the dissertation of Martin S. Frant, submitted in partial fulfillment of the requirements for the Ph.D. degree at Western Reserve University, February, 1953.

[3] Cliffdale Products Corp., Cleveland, Ohio.

[4] Gallowhur Chemical Corp., Ossining, N. Y.

[5] K. A. Kobe and T. F. Doumani, *Ind. Eng. Chem.*, **33**, 170 (1941).

[6] O. Dimroth, *Ann.*, **446**, 148 (1925).

[7] W. J. Klapproth and F. H. Westheimer, THIS JOURNAL, **72**, 4461 (1951).

[8] J. Jurgens, *Rec. trav. chim.*, **45**, 61 (1926).

[9] S. Coffey, *J. Chem. Soc.*, **127**, 1029 (1925).

[10] F. C. Whitmore, THIS JOURNAL, **43**, 619 (1921).

[11] O. Dimroth, *Ber.*, **35**, 2039 (1902).

[12] L. Vecchiotti, *Gazz. chim. ital.*, **44**, 34 (1914).

[13] F. C. Whitmore, "Organic Compounds of Mercury," Chemical Catalog Co. (Reinhold Publ. Corp.), New York, N. Y., 1921, p. 194.

[14] That the replacement of the acetoxymercuri group by halogen occurs without rearrangement has been widely accepted; *cf.* ref. 13, Chapter III, pp. 67–73; M. Kharasch and L. Chalkley, Jr., THIS JOURNAL, **43**, 607 (1921); A. Bernardi, *Gazz. chim. ital.*, **56**, 337 (1926).

[15] H. J. Lucas and N. F. Scudder, THIS JOURNAL, **50**, 245 (1928).

Nitrobromobenzene was recrystallized in the same manner from petroleum ether.

***o*-Bromobenzenesulfonic Acid.**—Seventeen grams of recrystallized *o*-aminobenzenesulfonic acid was diazotized in 100 ml. of 48% hydrobromic acid kept at 0°. The diazonium salt was decomposed with cuprous bromide, and the resulting solution filtered. The filtrate was made alkaline to remove most of the copper, and hydrogen sulfide passed in to remove the last traces.

The clear yellow solution was then concentrated on the steam-bath until sodium *o*-bromobenzenesulfonate precipitated out. The salt was collected, dried *in vacuo* over phosphorus pentoxide and ground with phosphorus pentachloride in a mortar. After the evolution of heat ceased, the mixture was poured over cracked ice. The heavy oil which collected on the bottom was extracted with ether. The ether was washed and then dried.

The dry ethereal solution was distilled under vacuum and the residual acid chloride divided into two portions. One was added to aqueous ammonia to form the amide (m.p. 182–183.5°, lit. 186°), as a means of identification, and the other hydrolyzed to the free acid.

***m*-Bromobenzenesulfonic Acid.**—This was prepared from Matheson metanilic acid in the same manner as the *ortho* compound. The amide melted at 149–152° (lit. 153°).

***p*-Bromobenzenesulfonic Acid.**—Eastman Kodak Co. *p*-bromobenzenesulfonyl chloride was recrystallized from petroleum ether (m.p. 74.3–75.1°) and refluxed in distilled water until hydrolysis was complete. The water and hydrogen chloride were removed by distillation under reduced pressure.

A sample of *p*-bromobenzenesulfonyl chloride was prepared from sulfanilic acid by the method described above. The identity of both samples was established by the melting points of the acid chloride (75–76°), and by conversion to the amide (m.p. 164–165°, lit. 166°). This was used as a further check on the reliability of the method of preparing the *ortho* and *meta* isomers.

Mercuration Reactions. Mercuration of *p*-Toluidine.[16]—Thirty-two grams (0.1 mole) of mercuric acetate was dissolved in the smallest possible amount of water, to which an equal volume of ethyl alcohol was added. Twelve grams (0.11 mole) of *p*-toluidine was dissolved in 200 ml. of alcohol, and the solution added to the above mercuric acetate solution. After two days at room temperature the mercurated product was removed by filtration. The yields averaged approximately 92% of theoretical.

An 11-g. sample of the dried mercuration product was added to 40 ml. of acetic anhydride and the mixture stirred for two days at 40°. Water was added to destroy residual acetic anhydride and then bromine in glacial acetic acid was added to the cold solution. After filtering off the precipitated mercuric bromide, hydrogen sulfide was passed in to remove the remaining mercuric ions. Over 97% of the mercury was recovered as bromide and sulfide. The solution was then made alkaline and extracted with chloroform. The over-all yield was 87%.

Melting Points of Isomeric Bromoacetylaminotoluenes.—The samples were weighed out on an analytical balance, and then ground together in a mortar. The melting points were taken in a specially adapted Thiele tube, in which both the sample and the thermometer were observed with magnifying lenses. The rate of increase of temperature was always less than one degree in five minutes.

Mercuration of Benzoic Acid.—Equal weights of mercuric acetate and primary standard benzoic acid were heated together at 130° for 1–1.5 hours. The cooled product was then treated with excess 20% bromine in glacial acetic acid, and an excess of aqueous sodium hydroxide added. The mercuric oxide was removed by filtration, and hydrogen sulfide passed through the solution to precipitate the last traces of mercuric ion. After filtration, the solution was made acid, whereupon most of the benzoic and bromobenzoic acids precipitated and were removed. The filtrate was then extracted several times with chloroform, the combined extracts added to the bulk of benzoic acids removed previously, and the chloroform evaporated to give the final product.

Infrared Determination of Isomeric Bromobenzoic Acids.—The isomeric bromobenzoic acids were analyzed by preparing working curves at 9.84, 10.00, 13.43 and 14.07 μ, using known materials, and determining the absorbancy of the unknown mixtures at these wave lengths. The solvent used throughout was anhydrous acetone, and the instrument was a Perkin–Elmer model 12C.

Mercuration of Nitrobenzene.—Eastman Kodak Co. White Label nitrobenzene was washed with dilute acid, dilute alkali and water. It was dried with anhydrous magnesium sulfate, and recrystallized twice at 4°. To 50 g. of nitrobenzene heated to 150° was added 10 g. of mercuric acetate over a period of 2.5 hours. It was felt that the amount of polymercuration might be reduced by the slow addition of mercuric acetate over a period of time. The mixture was kept at 150° for an additional 2.5 hours and then cooled. Excess 20% bromine in acetic acid was added to the chilled mixture and stirred for two hours. An equal amount of dioxane was then added, and hydrogen sulfide passed in. The solution was filtered and vacuum distilled at 1–2 mm. Di-*n*-butyl phthalate was added to the still-pot to serve as the highest-boiling fraction, and to prevent loss of product in the column. The first fraction was so taken as to include part of the nitrobenzene in the distillate.

Infrared Determination of Isomeric Bromonitrobenzenes.—The isomeric nitrobromobenzenes were analyzed in the same manner as the previous product. The wave lengths used were 10.01, 13.72, 13.83, 14.20 μ.

Mercuration of Benzenesulfonic Acid.—Benzenesulfonyl chloride was hydrolyzed in distilled water, and the water and hydrochloric acid removed by vacuum distillation. After several recrystallizations, the solid acid did not give a test for chloride ion. The acid melted at 43.5–46°.

A mixture of equal weights of benzenesulfonic acid and mercuric acetate was heated at 105° for two hours. The solution was allowed to cool, and excess bromine in 50% acetic acid was added. The temperature was raised gradually to 70° and bromine frequently added. The solution was then chilled, and mercuric bromide removed by filtration. Hydrogen sulfide was used to complete the removal of the mercury. The acetic acid, water and hydrogen bromide were then removed by vacuum distillation and the product dried in vacuum to produce a thick, sirupy liquid.

Infrared Determination of Isomeric Bromobenzenesulfonic Acids.—The mixture of bromobenzenesulfonic acids in acetone was analyzed by the standard base-line technique using a Perkin–Elmer model 12C instrument equipped with a potassium bromide prism. The following wave lengths were used: *ortho*, 9.84, 15.43; *meta*, 14.83, 15.32; *para*, 12.22, 13.61; the starting material (benzenesulfonic acid), 14.59.

Results

Cryoscopic Determination of Isomeric Bromoacetylaminotoluenes.—Mercuration of *p*-toluidine was investigated in order to ascertain the validity of the random attack hypothesis.[17] Use of a *para* disubstituted benzene with two groups of approximately the same size[18] simplifies the problem both sterically and statistically.

The melting points are given in Table I. From the results on the mixed melting points of unknown and known bromoacetylaminotoluenes, and the fact that no 2,4-isomer was ever isolated from a reaction product, it was concluded that the unknown product was predominantly 3,4-isomer. From the results of the mixed melting points of the known isomers, it was concluded that a minimum of 94% 3-bromo-4-acetylaminotoluene was present. Since the over-all yield in the reaction was 87%, the minimum yield of the isomer mercurated *ortho* to the amino group was 82%. The fact that one isomer is obtained almost exclusively would indicate that the concept of random attack is untenable in this case.

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(16) The method used is similar to that employed by L. Pesci, *Z. anorg. Chem.*, **17**, 281 (1898), and L. Vecchiotti, *Gazz. chim. ital.* **48**, II, 81 (1918). Neither author reported yields.

(17) W. J. Klapproth and F. H. Westheimer, ref. 7.

(18) L. Pauling, "Nature of the Chemical Bond," 2nd ed., Cornell University Press, Ithaca, N. Y., 1948, p. 164.

TABLE I

CRYOSCOPIC DETERMINATION OF ISOMERIC BROMOACETYLAMINOTOLUENES

	M.p., °C.
Unknown bromoacetylaminotoluene	109.9–114.0
Unknown + 5% 3-bromo-4-acetylaminotoluene	110.8–114.5
Unknown + 5% 2-bromo-4-acetylaminotoluene	104.5–114.8
100% 2-bromo-4-acetylaminotoluene	114.7–114.8
90% 3,4-isomer, 10% 2,4-isomer	106.5–115.1
92% 3,4-isomer, 8% 2,4-isomer	108.0–113.8
94% 3,4-isomer, 6% 2,4-isomer	109.1–115.1
96% 3,4-isomer, 4% 2,4-isomer	113.6–116.0
98% 3,4-isomer, 2% 2,4-isomer	116.2–117.0
100% 3-bromo-4-acetylaminotoluene	116.8–117.1

Infrared Analysis of Isomeric Bromobenzoic Acids.—In all, there were four determinations on the benzoic acid isomers using two independent sets of working curves. In each case two separate samples of unknown, at different concentrations, were used. The results are recorded in Table II.

TABLE II

RESULTS OF MERCURATION OF BENZOIC ACID

	Average of 4 runs
Benzoic acid remaining in mixture, %	59
Isomeric bromobenzoic acids, %	41
Ortho isomer in product	57
Meta isomer in product	25
Para isomer in product	18

No prior worker has reported any *meta* or *para* isomer from the mercuration of benzoic acid. The failure to report these isomers apparently is due to the difficulties encountered in fractionally crystallizing the bromobenzoic acids, as well as the possibility of losing them entirely in attempting to isolate a mercurated "anhydride"[19] in the course of purifying the mercurated benzoic acid.

These results, like those for *p*-toluidine, would seem to indicate that the mercuration process is not one of random attack, and that some directing influence, whatever its nature, must be present.

Infrared Analysis of Isomeric Nitrobromobenzenes.—In all, three unknowns at three different wave lengths were run and the results are given in Table III.

TABLE III

RESULTS OF MERCURATION OF NITROBENZENE

	Average of 3 runs
Nitrobenzene remaining in mixture, %	42
Ortho isomer in product	53
Meta isomer in product	32
Para isomer in product	15

There have been other published reports of the results of the mercuration of nitrobenzene. These are summarized in Table IV. As can be seen, the present authors report a higher percentage of *para* and a lower percentage of *meta* than previously noted. There are several possible reasons for this difference.

TABLE IV

MERCURATION OF NITROBENZENE BY MERCURIC ACETATE

Literature reference	Analytical method	Results
[a]	Recrystn. and isolation	Only *ortho*
[b]	Competitive reacn. of bromo cmpds.	*Ortho, para* 57–60 *Meta* 40–43
[c]	Ternary melting point	*Ortho* 53 *Meta* 38 *Para* 9
[d]	Competitive reacn. of bromo cmpds.	*Ortho, para* 57 *Meta* 43
[e]	Infrared spectroscopy	*Ortho* 53 *Meta* 32 *Para* 15

[a] O. Dimroth, *Ber.*, **35**, 2036 (1902). [b] O. Dimroth, *Ann.*, **446**, 148 (1925). [c] J. Jurgens, *Rec. trav. chim.*, **45**, 61 (1926). [d] W. J. Klapproth and F. H. Westheimer, ref. 7. [e] Present work.

One reason may be that the results given in Table IV are not strictly comparable. All were run at 150° but for varying lengths of time, the reaction generally not being permitted to go to completion in order to avoid polymercuration. In the present work, the mercuric acetate was added very slowly to achieve the same result, and allowed to run for a longer time. A longer reaction time favors the establishment of equilibrium conditions, which would be important if all three isomers are not equally stable.

Secondly, it is felt that inherently the infrared technique is superior to those previously used. The chemical competition method[20] requires the isolation of the mercurated material, and the recovered product is washed with both polar and nonpolar solvents to free it of mercuric acetate and nitrobenzene. There are no available data on the relative solubilities of the various isomers. Similarly, in the case of a ternary melting point technique, the mercurated material and the corresponding bromo compounds must be kept free of even minor impurities. On the other hand, using absorption spectroscopy, impurities which do not absorb at the same wave length as the desired component are of little concern.

All of the work on the classical mercuration of nitrobenzene, however, indicates an unusual fact: one does not obtain the isomer ratio to be expected by inference from bromination, nitration, sulfonation or similar reactions.

Infrared Analysis of the Isomeric Bromobenzenesulfonic Acids.—The results of the analysis of the isomeric bromobenzenesulfonic acids are given in

TABLE V

INFRARED ANALYSIS OF ISOMERIC BROMOBENZENESULFONIC ACIDS

	Ortho	*Meta*	*Para*	Starting material	Total
Normality	0.040	0.102	0.025	0.018	0.35
Distribution, %	24	61	15	. . .	. .

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[19] F. C. Whitmore, ref. 13, pp. 290–292.

[20] *o*- and *p*-bromonitrobenzenes react with piperidine; *m*-bromonitrobenzene does not, according to W. J. Klapproth and F. H. Westheimer, ref. 7.

Table V. The accuracy of the determination was checked by adding the individual normalities of the acids and comparing the result with a total normality determined by titration with standard base. Agreement was within 3%.

The ratio of starting material to final product indicates that the reaction goes virtually to completion. The difference in the rate and extent of reaction between benzenesulfonic acid, on the one hand, and nitrobenzene and benzoic acid, on the other, as well as the marked difference in the isomer ratios obtained, may well indicate a different mechanism of attack.

OSSINING, N. Y.

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF JOHNS HOPKINS UNIVERSITY AND THE PATHOLOGY DEPARTMENT OF GEORGETOWN UNIVERSITY]

Some N-Alkylsaccharin Derivatives[1]

BY E. EMMET REID, LEONARD M. RICE AND CHARLES H. GROGAN

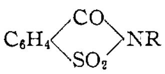
RECEIVED NOVEMBER 4, 1954

The series of N-alkylsaccharins has been extended to eicosyl. Along with these five ω-cyano and two ω-hydroxy derivatives have been made. Polymethylene-bis-saccharins from methylene to decamethylene have been prepared and characterized. Three N-alkylsulfamic acids have been obtained by opening the rings of N-alkylsaccharins with alkali.

In a recent paper[2] we reported the preparation of a number of N-alkylsaccharins, using dimethyl formamide as a solvent. Since then the use of this solvent and the preparation of several of the same compounds have been reported by Rice and Pettit.[3] We have extended the series of substituted saccharins up to eicosyl and added five cyanoalkyl and two hydroxyalkyl derivatives. In addition we have prepared the polymethylene-bis-saccharins up to the decamethylene and several in which the polymethylene chain is interrupted by oxygen or sulfur atoms.

TABLE I

N-ALKYLSACCHARINS



$C_6H_4\left\langle\begin{matrix}CO\\SO_2\end{matrix}\right\rangle NR$

R	Formula	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
Tridecyl	$C_{20}H_{31}O_3NS$	44.8	65.71	65.69	8.55	8.53	...	...
Tetradecyl[a]	$C_{21}H_{33}O_3NS$	60	66.45	66.66	8.76	8.75	...	...
Pentadecyl	$C_{22}H_{35}O_3NS$	53.5	67.13	67.31	8.96	9.36	...	...
Cetyl[a]	$C_{23}H_{37}O_3NS$	67	67.77	68.00	9.15	9.32	...	...
Heptadecyl	$C_{24}H_{39}O_3NS$	60.5	68.36	68.51	9.32	9.59	...	...
Octadecyl[a]	$C_{25}H_{41}O_3NS$	73	68.92	69.28	9.51	9.27	...	...
Nonadecyl	$C_{26}H_{43}O_3NS$	65	69.44	69.68	9.64	9.69	...	...
Eicosyl	$C_{27}H_{45}O_3NS$	76.5	69.94	70.27	9.79	9.97	...	...
$-CH_2CN$	$C_9H_6O_3N_2S$	144	...	...	..	..	12.61	12.81
$-(CH_2)_2CN$	$C_{10}H_8O_3N_2S$	148	...	...	..	..	11.86	11.89
$-(CH_2)_3CN$	$C_{11}H_{10}O_3N_2S$	105	...	...	..	..	11.19	10.87
$-(CH_2)_4CN$	$C_{12}H_{12}O_3N_2S$	98	...	...	..	..	10.60	10.21
$-(CH_2)_5CN$	$C_{13}H_{14}O_3N_2S$	50	...	...	..	..	10.07	10.33
$-(CH_2)_2OH$	$C_9H_9O_4NS$	108	47.57	47.70	3.99	4.29	6.16	5.93
$-(CH_2)_3OH$	$C_{10}H_{11}O_4NS$	74	49.78	50.02	4.60	4.66	...	...

[a] Made by Rice and Pettit who give the melting points 52.5–54.5°, 63–65 and 68–71°.

The preparation of N-alkylsaccharins has been recommended by Merrit, Levy and Cutter[4] for the identification of alkyl halides. They used Carbitol as a solvent. Dimethylformamide is more convenient. If it is desired to identify the halogen as well as the alkyl, the sodium halide may be filtered off from the hot reaction mixture before it is poured into water.

The melting points and analyses of the mono-N-alkylsaccharins are in Table I and the melting points are plotted in Fig. 1. The melting points from hexyl to dodecyl are from our previous paper[2] and those of the lower members from the literature. The melting point pattern is of interest as it characterizes the series. It is important since its regularity is a far more rigid criterion of the purity of the compounds than analyses. This series is unusual in that the swing of the alternation increases from the nonyl up. There is a reversal of phase at the nonyl.

For comparison the melting points of the O-alkylsaccharin derivatives[5] are plotted along with the N-alkyl in Fig. 1. When the oxygen atom is considered a member of the alkyl chain the melting point patterns are remarkably similar from the nonyl on.

Two hydroxy compounds, N-β-hydroxyethyl and N-γ-hydroxypropyl, were prepared from the corre-

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[1] Supported in part by the Geschickter Fund for Medical Research.

[2] L. M. Rice, C. H. Grogan and E. Emmet Reid, THIS JOURNAL, **75**, 4304 (1953).

[3] H. L. Rice and G. R. Pettit, *ibid.*, **76**, 302 (1954).

[4] L. L. Merritt, Jr., Stanley Levey and H. B. Cutter, *ibid.*, **61**, 15 (1939).

[5] J. R. Meadow and E. Emmet Reid, *ibid.*, **65**, 457 (1943).