heating the contents of B and cooling was repeated three times, the same result was obtained in each case, showing that during the heating of B, no decomposition or changes took place which effected the color of the recooled solution to the naked eye.

**Thermochromic Changes of Ethyl Benzoate Solutions of IIIb** (Ar = $C_6H_5$).—Twenty ml. of the above solution was divided into two equal parts and placed in two Schlenk tubes (A and B) as described above. A was placed in an ice-bath and the level of the solution was marked. A and B were then heated (bath temp., 170°) for three minutes and the level of the solution in A was marked (C). On cooling (ice-bath), ethyl benzoate was added to A to bring the level of the solution to mark C and then A and B were sealed in a stream of dry pure nitrogen. B was heated to 170° for three minutes, when the solution acquired an orange color, compared with the violet-brown color of the cold solution in (A) (ice-bath). This experiment was repeated three times with the same result. When B was cooled in ice, the color of the solutions in A and B were of the same shade, but the intensity of the color was a little less in A, owing to the fact that the solution in B at 0° is more concentrated than that in A, whereas the concentrations of both solutions are the same at 170°.

Experiments similar to those carried out with IIIb (Ar = $C_6H_5$) were carried out with IIIb (Ar = $p$-$CH_3OC_6H_4$-) giving similar results.

**Action of Phenylmagnesium Bromide on I.**—To a Grignard solution (prepared from 0.8 g. of magnesium, 6 g. of bromobenzene and 40 ml. of dry ether) was added 1 g. of I and 30 ml. of dry benzene. The resulting deeply violet colored reaction mixture was refluxed (water-bath) for two hours and kept aside overnight at room temperature. It was decomposed with cold saturated aqueous ammonium chloride solution and the resulting blue-violet precipitate was filtered off, washed with water and finally with cold alcohol. This was identified as IIa through the formation of the corresponding diacetate (IIc) (m.p. and mixed m.p.[2]); yield is *ca.* 60%.

**Action of Ethereal Diazomethane Solution on I.**—To a suspension of 1 g. of (I) in 50 ml. of dry ether was added an ethereal solution of diazomethane (prepared from 4 g. of nitrosomethylurea) and the reaction mixture was kept at 0° overnight and then treated with a fresh amount of ethereal diazomethane. During the reaction, the yellow solid I was gradually transformed into a pale yellow substance which was collected and crystallized from glacial acetic acid as pale yellow crystals, m.p. 228°. *Anal.* Calcd. for $C_{17}H_{10}N_2O_2$ requires C, 74.5; H, 3.6; N, 10.2. Found: C, 74.2; H, 3.7; N, 10.5. IV is difficultly soluble in benzene and ethyl alcohol and dissolves in concentrated sulfuric acid with a bluish-green color.

A solution of 0.2 g. of IV in 30 ml. of glacial acetic acid was treated with 0.5 ml. of concentrated hydrochloric acid and the reaction mixture was heated on a boiling water-bath for 15 minutes. It was then poured into ice-cold water and the blue-violet solid that separated was filtered off, washed with cold alcohol and identified as IIc as mentioned above.

CAIRO, EGYPT

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[CONTRIBUTION FROM THE GEORGETOWN UNIVERSITY MEDICAL CENTER]

# N-Alkyl Saccharins and their Reduction Products

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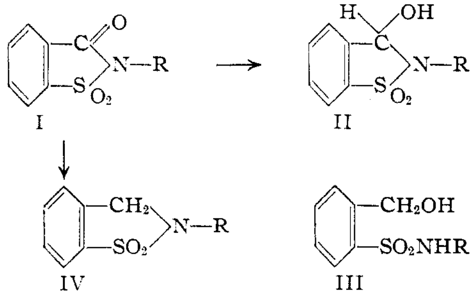
RECEIVED MARCH 12, 1953

The series of N-alkyl saccharins has been extended through dodecyl and representative members of the series have been reduced with lithium aluminum hydride. The reduction products were isolated and characterized chemically and by their infrared spectra. The products turned out unexpectedly to be N-alkyl derivatives of *o*-methylolbenzenesulfonamide. Dimethylformamide was found to be an excellent solvent for the synthesis of N-alkyl saccharins from the sodium saccharin salt and appropriate alkyl halides.

As part of a continuing study of the reduction of amides, we have extended the investigation of types of amides to include the N-alkyl saccharin, I, and have studied their reduction by means of lithium aluminum hydride. The N-alkyl saccharins, methyl through amyl, had been prepared previously by the reaction of sodium saccharin with an alkyl halide employing as a solvent a mixture of water and butyl carbitol.[2]

The series of N-alkyl saccharins has been extended from hexyl through dodecyl utilizing dimethylformamide as a solvent for the sodium saccharin salt. Just below its boiling point dimethylformamide dissolves about two-thirds of its weight of sodium saccharide, and it is a fair solvent for alkyl bromides. These saccharin derivatives were low melting solids which could be readily purified by vacuum distillation. The compounds prepared in this study and appropriate constants are shown in Table I.

It was of interest to study the behavior of these compounds on reduction with lithium aluminum hydride. Preliminary experiments indicated that the sulfone group was not reduced under the conditions employed and that all reduction observed took place at the carbonyl group. Reduction of the N-dodecyl derivative went smoothly and gave a product which, after recrystallization from benzene–petroleum ether, melted at 84°. Analysis, however, showed that no oxygen had been lost during the reduction. Since reduction of the sulfone group does not occur, partial or complete reduction of the carbonyl function gives three possibilities for the course of the reaction. These, as shown by formulas II, III and IV, are: partial reduction to yield a cyclic secondary alcohol, partial reduction with ring cleavage to yield a primary alcohol, and complete reduction to yield a ring methylene group as originally expected.



In all cases of representative members of this series studied, the sulfone group was unaffected and

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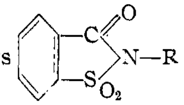
[2] L. L. Merritt, Jr., Stanley Levey and H. B. Cutter, THIS JOURNAL, **61**, 15 (1939).

TABLE I

N-ALKYL SACCHARINS



| R | Formula | M.p., °C. | B.p. °C. | B.p. Mm. | Carbon Calcd. | Carbon Found | Hydrogen Calcd. | Hydrogen Found | Nitrogen Calcd. | Nitrogen Found |
|---|---|---|---|---|---|---|---|---|---|---|
| Hexyl | $C_{13}H_{17}NSO_3$ | 17–19 | 145–150 | 0.2 | 58.40 | 58.43 | 6.41 | 6.21 | 5.24 | 5.17 |
| Heptyl | $C_{14}H_{19}NSO_3$ | 37–38 | 150–153 | .3 | 59.76 | 59.95 | 6.81 | 6.60 | 4.98 | 5.04 |
| Octyl | $C_{15}H_{21}NSO_3$ | 20–22 | 160–162 | .3 | 60.99 | 61.10 | 7.17 | 7.14 | 4.74 | 4.67 |
| Nonyl | $C_{16}H_{23}NSO_3$ | 30–30.5 | 158–162 | .2 | 62.10 | 62.27 | 7.49 | 7.17 | 4.53 | 4.94 |
| Decyl | $C_{17}H_{25}NSO_3$ | 35–36 | | | 63.12 | 63.43 | 7.79 | 7.83 | 4.33 | 4.48 |
| Undecyl | $C_{18}H_{27}NSO_3$ | 38–39 | 175–185 | .1 | 64.06 | 64.24 | 8.07 | 7.84 | 4.15 | 4.36 |
| Dodecyl[a] | $C_{19}H_{29}NSO_3$ | 48–49 | | | 64.92 | 65.18 | 8.32 | 8.12 | 3.99 | 4.04 |

[a] H. W. Arnold and N. E. Searle, U. S. Patent 2,462,835 (March, 1949).

the carbonyl group was reduced to the alcohol level only with ring cleavage yielding product III. The incomplete reduction of the carbonyl group in this type amide, which was not expected, must be attributed to the influence of the sulfonamide bonding on the carbonyl group.

The presence of the hydroxyl group was demonstrated by conversion into the acetate and analysis. The reduction products of the N-alkyl saccharins are soluble in sodium hydroxide solution; acidification of these solutions causes the products to precipitate unchanged. This is characteristic of sulfonamides in which there is a hydrogen on the nitrogen.

The N-hexyl and N-heptyl derivatives, when similarly reduced, yielded products which when analyzed agreed with the calculated values for structure III.

To obtain additional evidence as to the structure of the reduction products infrared absorption curves were run. The graph of the infrared absorption spectrum of N-dodecyl saccharin before reduction showed no bands in the region 2.5–3.20 $\mu$ attributable to stretching vibrations characteristic of NH or OH groupings. There was also evident the characteristic peak at 5.80 $\mu$ due to the carbonyl group.

The corresponding graph for the reduced dodecyl saccharin showed 2 peaks in the region 2.5–3.2 $\mu$ which is evidence for ring opening with the formation of an OH and NH group. The carbonyl band at 5.8 $\mu$ in this case has completely disappeared indicating its reduction.

The graph of the acetate of the reduced dodecyl saccharin showed only one peak in the region 2.5–3.20 $\mu$ which is presumably due to the NH group since the OH has been converted to acetate. In addition, in the region 5.8 $\mu$ there is a reappearance of the carbonyl band. There was also the appearance of a new band in the 8.2 $\mu$ region due to the acetate grouping.

## Experimental

**Preparation of N-Alkyl Saccharins.**—Hydrated sodium saccharin, 48 g. (0.2 mole), was dissolved by heating in 75 ml. of dimethylformamide. Slightly less than the calculated amount of the alkyl bromide was added to the hot solution. The mixture was heated at reflux 1 to 2 hours in an oil-bath. Separation of sodium bromide was observed within a few minutes. The reaction mixture was poured into 200 ml. of water. The product separated as a heavy oil which was washed with water by decantation. This method was used for the decyl, undecyl and dodecyl members. The others were made in the same manner except that 100 ml. of solvent was used for approximately the same amount of the sodium salt; and the alkyl bromide, dissolved in two volumes of dimethylformamide, was added gradually through the condenser. The mixture was refluxed for several hours and poured into 1 liter of water.

The decyl and dodecyl compounds solidified and were recrystallized from 30–60° petroleum ether. The others were dried by heating *in vacuo* and distilled.

**Reduction of N-Alkyl Saccharins.**—A solution of 10 g. of N-alkyl saccharin in 200 ml. of anhydrous ether was added with stirring to a solution of 1 g. of $LiAlH_4$ in 400 ml. of dry ether. After the addition was completed, the mixture was stirred for 2 hours. Water was then added until the evolution of hydrogen ceased; and then a slight excess added. The inorganic solids were filtered off and the ether solution dried over anhydrous sodium sulfate. The ether was stripped off and the products recrystallized from benzene–petroleum ether.

The N-hexyl-, N-heptyl- and N-dodecylsaccharin derivatives were reduced as described with the following results.

***o*-Methylol-N-hexylbenzenesulfonamide.**—Recrystallized from benzene–petroleum ether, m.p. 55°. *Anal.* Calcd. for $C_{13}H_{21}NO_3S$: C, 57.53; H, 7.80; N, 5.16. Found: C, 57.88; H, 7.53; N, 5.29.

***o*-Methylol-N-heptylbenzenesulfonamide.**—Recrystallized from benzene–petroleum ether, m.p. 61°. *Anal.* Calcd. for $C_{14}H_{23}NO_3S$: C, 58.91; H, 8.12; N, 4.91. Found: C, 59.15; H, 8.21; N, 5.22.

***o*-Methylol-N-dodecylbenzenesulfonamide.**—Recrystallized from benzene-petroleum ether, m.p. 84°. *Anal.* Calcd. for $C_{19}H_{33}NO_3S$: C, 64.19; H, 9.36; N, 3.94; O, 13.50; S, 9.02. Found: C, 64.53; H, 9.34; N, 3.93; O, 13.24; S, 9.04.

***o*-Acetoxymethyl-N-dodecylbenzenesulfonamide.**—The acetate of the reduced dodecylsaccharin was prepared in the usual way by means of acetyl chloride. The product was recrystallized from ethanol, m.p. 64°. *Anal.* Calcd. for $C_{21}H_{35}NO_4S$: C, 63.44; H, 8.87; N, 3.52; O, 16.12; S, 8.06. Found: C, 63.44; H, 8.66; N, 3.80; O, 16.09; S, 7.96.

**Acknowledgment.**—We are indebted to Mr. Meyer Dolinsky and Mr. Jonas Carol of the Food and Drug Administration, Federal Security Agency, Washington, D. C., for the infrared spectra.

WASHINGTON, D. C.