tallization was accomplished by dissolving the sirup in a small volume of water and adding 3 volumes of alcohol followed by acetone until a faint turbidity was observed. Long needles (about 10 g.) were deposited after standing overnight in the refrigerator. The crude material was recrystallized for analysis from water–alcohol–acetone mixture, $[\alpha]^{28}D$ +96.4° (2% in water).

Anal.[7] Calcd. for $C_8H_{14}O_5NCl$: C, 33.42; H, 6.54; N, 6.50; Cl, 16.44. Found: C, 33.58; H, 6.45; N, 6.59; Cl, 16.40.

It is of interest that the hexosamines are eluted from the resin[8] before the amino acids,[9] suggesting that the mechanism of action in either or both cases is not simple ion exchange. The separation of glucosamine from amino acids by this procedure was tested by adding inactive glucosamine hydrochloride to radioactive amino acids. The isolated glucosamine hydrochloride possessed less than 0.5% of amino acid contamination. The details of these experiments will be presented elsewhere.

N-Acetyl-D-glucosamine.—A solution containing 43.2 g. of glucosamine hydrochloride (Nutritional Biochemicals Corp.) in 1 l. of water and 100 ml. of methanol was stirred for 90 minutes at 0–5° with 1200 ml. of Dowex-1, carbonate form and 26 ml. of acetic anhydride. The mixture was filtered and the filtrate and washings were passed through a column containing 200 ml. of Amberlite IR-120, acid form.[6] The colorless effluent and washings were heated to boiling and the solution was concentrated to dryness *in vacuo* with the temperature of the water-bath below 55°. The N-acetyl-D-glucosamine crystallized during this procedure as white needles (40 g.), m.p. 193–195° (dec., preliminary browning). Recrystallization could be effected as described by White.[10] Better results were obtained by dissolving the crude material (37 g.) in water (100 ml.) and ethanol (75 ml.), heating the solution on the steam-bath and gradually adding, with vigorous stirring, 1 l. of boiling dimethoxyethane (Arapahoe Chemicals Co.). The major portion of the purified compound crystallized out of the boiling solution as long, colorless needles. After slow cooling, 32 g. of product was obtained, m.p. 210° (dec., turns tan at about 203°), $[\alpha]^{28}D$ +41.0° (*c* 1.0, water, final). Additional material (about 2 g.) was obtained from the mother liquors.

Anal.[7] Calcd. for $C_8H_{15}O_6N$: C, 43.43; H, 6.84; N, 6.33. Found: C, 43.43; H, 7.02; N, 6.37.

The silver acetate–methanol procedure was reported to yield products melting at 190°[11] and 196°.[10] When obtained by acyl migration during methanolysis of 1,3,4,6-tetraacetyl-D-glucosamine, however, the compound was reported to melt at 205°.[12] This is confirmatory evidence that the silver acetate procedure yields impure preparations.

N-Acetyl-D-galactosamine.—Chondrosamine hydrochloride was treated as described for glucosamine hydrochloride. Concentration of the final solution to dryness gave a sirup which was readily crystallized by the addition of a little absolute ethanol; yield was from 85–95%, m.p. varying from 162 to 171°. Recrystallization of the product was unsatisfactory since losses were appreciable, although second and third crop material could be recovered from the mother liquors. The solvent system employed was the usual methanol–ethyl acetate mixtures. The purified product melted at 172–173° (preliminary softening), $[\alpha]^{27}D$ +86.1° (*c* 1.0, water, final). The m.p. varied about 3° (higher or lower) depending upon the rate of heating.

Anal.[7] Calcd. for $C_8H_{15}O_6N$: C, 43.43; H, 6.84; N, 6.33. Found: C, 43.68; H, 6.88; N, 6.13.

Previous reports on the physical constants of the compound as obtained by the silver acetate method were: m.p. 120–122°, $[\alpha]^{21}D$ +80° (equil.)[13]; m.p. 154°[14]; m.p. 159–160°, $[\alpha]^{5}D$ +94.5° (equil.)[15]; m.p. 162–164° (uncor.), $[\alpha]_{5461}$ +98° (equil.).[16] The suggestion[13] that the low melting compound was a hydrate is of interest since the compound isolated from aqueous solution by the present procedure is high melting and anhydrous.

It was reported[16] that the N-acetylhexosamines showed very similar R_f values in a wide variety of solvents. Investigations in this Laboratory confirmed this point, although small differences in R_f (about 5–8%) were noted when butanol–pyridine–water mixtures (6:4:3; upper phase) were used with Whatman #1 paper.

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An Improved Procedure for the Preparation of Alkyl Halide Derivatives of Saccharin

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The preparation of alkyl derivatives of saccharin (I) by using the sodium salt of saccharin with an alkyl halide has been accomplished previously by methods which have resulted in poor yields,[3–6] and which generally required a long reaction time. The work of Sheehan and Bolhofer[7] suggested to us that the poor yields obtained by previous workers might have been due to an inadequate solvent. Sheehan described the preparation of alkyl phthalimides from the halide and sodium salt using a dimethylformamide solvent. Recently many alkyl 4-nitrophthalimides have been prepared by Billman and Cash[8] using the same solvent.

Our own work, these previous reports, and an unpublished observation by Stacy and Gortatowski[9] have led us to believe that dimethylformamide is especially effective as a solvent for weakening halogen carbon bonds. Its activating influence appears to extend beyond its powerful solvating ability into the realm of catalysis.

In our investigations dimethylformamide has been found to be an excellent solvent for the reaction of alkyl halides with sodium saccharin. Previous investigators have not reported exact yields for individual derivatives but they appeared

(1) E. I. du Pont, Electrochemicals Department, Niagara Falls, N. Y.

(2) This work was carried out by George R. Pettit as an undergraduate research project.

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(9) G. W. Stacy and M. Gortatowski observed that alkylation occurred swiftly and practically quantitatively between *p*-nitrobenzyl chloride and a sodium enolate in dimethylformamide.

TABLE I

N-ALKYLSACCHARIN DERIVATIVES

RX	Yield, %[a]	M.p., °C.[b]	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
Methyl iodide	94	131–132(132)[c]							
Ethyl bromide	70	93.5–94.5(94)							
n-Butyl chloride	52	39–40(38)							
s-Butyl chloride[d]	13	80–81(81)							
n-Heptyl iodide	40	37.5–38.5	$C_{14}H_{19}NO_3S$	59.75	59.52	6.80	6.71	4.98	4.79
n-Decyl bromide	59[h]	35–36	$C_{17}H_{25}NO_3S$	63.12	62.91	7.79	7.86	4.33	4.14
n-Undecyl bromide	16[h]	38.5–39.5	$C_{18}H_{27}NO_3S$	64.05	63.99	8.07	8.25	4.15	4.14
n-Dodecyl bromide	64	48–50(51)[e]							
n-Tetradecyl bromide	94	52.5–54.5	$C_{21}H_{33}NO_3S$	66.46	66.56	8.76	8.75	3.69	3.59
n-Hexadecyl bromide	90	63–65	$C_{23}H_{37}NO_3S$	67.80	67.66	9.15	9.15	3.43	3.47
n-Octadecyl bromide	86	68–71	$C_{25}H_{41}NO_3S$	68.95	69.21	9.49	9.56	3.21	3.12
β-Phenylethyl bromide	68	138–139[f]	$C_{15}H_{13}NO_3S$	62.72	62.66	4.56	4.65	4.87	4.93
Allyl chloride	66	89–90(94)[e]							
Benzyl chloride	92	110–111(111)							
o-Chlorobenzyl chloride	94	166–167	$C_{14}H_{10}ClNO_3S$	54.63	54.39	3.28	3.17	4.55	4.64
p-Chlorobenzyl chloride	95	157–159[g]	$C_{14}H_{10}ClNO_3S$	54.63	54.82	3.28	3.22	4.55	4.52

[a] Yields indicated are based on the crude product obtained unless otherwise stated. [b] Melting point of analytical sample; analytical samples were recrystallized three to six times from isopropyl alcohol unless otherwise stated. [c] Melting points in parentheses are those reported by Merritt, *et al.* (ref. 3) unless otherwise stated. [d] It had been reported (ref. 3) that a derivative could not be obtained with *s*-butyl chloride in accordance with the procedure given, although the bromide and iodide did furnish derivatives. [e] As reported by H. W. Arnold and N. E. Searle, U. S. Patent 2,462,835; *C. A.*, **43**, 4421 (1949). [f] Recrystallized from a mixture of petroleum ether (b.p. 30–50°) and acetone. [g] Recrystallized from a mixture of petroleum ether (b.p. 30–50°) and ethyl acetate. [h] Yield of once recrystallized material.

to vary from 6 to 35% for methyl, ethyl, *n*-butyl, allyl and benzyl derivatives when Butyl Carbitol was the solvent. Our yields for the preparation of the same derivatives varied from 52–94% (Table I). The saccharin derivative from *s*-butyl chloride had not been obtained using Butyl Carbitol as a solvent,[3] but it is easily prepared by the use of dimethylformamide.

An increase in the yield of N-alkylsaccharin derivatives was noticed by Merritt, *et al.*,[3] when potassium iodide was used in the reaction of sodium saccharin with alkyl chlorides. In our work sodium iodide also was found to bring about increased yields for all reactions involving alkyl chlorides.

The reaction is usually complete after 30 minutes when carried out at temperatures of from 90–150°. Derivatives could not be obtained from *t*-butyl bromide, cyclohexyl iodide, *p*-nitrobromobenzene, or N-bromosuccinimide. Isoamyl bromide, *n*-hexyl bromide, *n*-octyl bromide, and *n*-nonyl bromide give derivatives which did not crystallize from isopropyl alcohol. Longer chain halides gave saccharin derivatives which were difficult to purify. The clean, rapid reactions experienced with dimethylformamide do, however, make it possible to work with lower melting point derivatives with a minimum of difficulty. All derivatives prepared along with pertinent information have been recorded in Table I.

Experimental[10]

Preparation of N-Alkylsaccharin Derivatives. Procedure A. N-*n*-Decylsaccharin.—Sodium saccharin (11.0 g., 0.046 mole) was added to a solution of 5.0 g. (0.023 mole) of *n*-decyl bromide in 50 ml. of dimethylformamide contained in a round-bottomed flask fitted with a reflux condenser. The mixture was heated on a steam-bath for 30 minutes with occasional shaking. The mixture was diluted with water and extracted with several portions of chloroform. Evaporation of the chloroform, after drying over anhydrous sodium sulfate, produced a residue which was crystallized from isopropyl alcohol.

Procedure B. N-*o*-Chlorophenylsaccharin.—Fifteen grams (0.062 mole) of sodium saccharin and 9.3 g. (0.062 mole) of sodium iodide were added to a solution of 5.0 g. (0.031 mole) of *o*-chlorobenzyl chloride in 50 ml. of dimethylformamide. The mixture was heated on a steam-bath for 30 minutes.

Upon dilution with water a light yellow, crystalline product separated. The mixture was extracted with several portions of chloroform. The combined extracts were washed with sodium bisulfite to remove iodine, once with water, and then dried over anhydrous sodium sulfate. The residue obtained upon evaporation of the chloroform was recrystallized from isopropyl alcohol.

The less reactive, normal and branched chained alkyl chlorides were found to give best yields when the reaction was carried out at 150°.

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(10) All melting points are corrected. The microanalytical work was performed by the Galbraith Laboratories, Knoxville, Tennessee.

The Synthesis of N,N-Bis-(β-diethylaminoethyl)-amine and Some N-Substituted Alkanesulfonamides

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A new and potentially useful amine intermediate, N,N-bis-(β-diethylaminoethyl)-amine, has been synthesized. The synthesis of this compound has led to the preparation of certain N-substituted alkanesulfonamides. In addition to sulfonamides that incorporate the above amine moiety, a number of other N-substituted alkanesulfonamides