from the corresponding nitroethenes. To check this conclusion the saturated compounds were dehydrohalogenated by treatment with sodium acetate[22] in anhydrous ether, the olefins isolated in pure form, and their chromatographic peaks determined. In both cases the peaks obtained corresponded in elution time to the peaks observed in the original product mixtures. The following example illustrates the procedure employed:

Sodium acetate, 3.6 g (0.035 mole), was slowly added with stirring to a solution of 1,1,1,2-tetrachloro-2-nitroethane, 6.4 g. (0.03 mole), in anhydrous ether, 15 ml., at 0°. After 1 hr., the solution was filtered to remove excess sodium acetate and sodium chloride, and the ether and acetic acid removed under reduced pressure. Distillation gave 1,2,2-trichloronitroethylene, 4.1 g. (77.5% yield), b.p. 55° (4 mm.).

A Perkin-Elmer Vapor Fractometer with a 2-meter stainless steel column containing Celite packing coated with dodecyl phthalate, a temperature of 140°, and a flow rate of 20 cc. of helium per min. were used to determine the gas chromatographic peaks. Applications of gas chromatography to analysis of nitroparaffin mixtures have been discussed more fully by Bethea and Wheelock.[31]

1-Chloro-2-bromonitroethane identification and reactions. The product from the vapor phase reaction of vinyl chloride with nitrogen dioxide and bromine showed the following constants: b.p. 68° (6.7 mm.), n_D^{20} 1.4970. The anthranilic acid derivative melted at 139–140° and showed a mixture m.p. of 139–140° with the same derivative from 1,2-dichloronitroethane. Hydrolysis with 88% sulfuric acid for 5 hr. gave a 40% yield of bromoacetic acid, b.p. 66–67° (1.0 mm.), m.p. 50°

Nitrohalogenation of the enol acetate of methyl ethyl ketone. (We are indebted to Dr. Takeo Hokama for conducting these experiments.) 2-Buten-2-yl acetate, 23 g. (0.2 mole), was added dropwise in about 2 hr. to a solution of the nitrohalogenating agent (0.2 mole) in 100 ml. of carbon tetrachloride at ice bath temperatures. After stirring for an additional hour the mixture was washed with 10% urea solution, and water, and then dried and distilled. The products were as follows:

Nitrohalogenating Agents	Products (% yld.)	Properties
$N_2O_4 + Cl_2$	3-Chlorobutanone (58)	B.p. 40° (45 mm.)
$N_2O_4 + Br_2$	3-Bromobutanone (50)	B.p. 52° (30 mm.)
NO_2Cl	3-Nitrobutanone (36)	B.p. 56° (2 mm.)

They were further characterized by preparation of derivatives whose properties coincided with those reported in the literature.[32]

LAFAYETTE, IND.

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[CONTRIBUTION FROM BIOCHEMICAL LABORATORY, COLLEGE OF AGRICULTURE, KYOTO UNIVERSITY]

N-Acylation of Unsubstituted Glycosylamines

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N-Monoacylation of unsubstituted glycosylamines has been conveniently achieved by the reaction with acid anhydride in *N*,*N*-dimethylformamide or in methanol. *N*-Acetyl-α-D-arabinopyranosylamine, -β-D-xylopyranosylamine, and -β-D-glucopyranosylamine, *N*-benzoyl-β-D-xylopyranosylamine, and a series of *N*-acyl-β-D-glucopyranosylamines with even-numbered fatty acids as the acyl group have been prepared by these methods in good yields.

N-Monoacetylglycosylamines have been prepared by partial hydrolysis of fully *O*-acetylated derivatives of *N*-acetylglycosylamines,[1-4] or by the reaction of unsubstituted glycosylamines and ketene.[5,6] They have also been formed by the action of ammonia on acetylated sugars,[7,8] acetylated aldehydo-sugars,[7,9] or acetylated glyconononitriles.[9,10] *N*-Benzoyl-D-mannosylamine, apparently the only reported *N*-monobenzoyl derivative of glycosylamine, has been formed in a small yield by the reaction of D-mannose cyanohydrin hexabenzoate with silver nitrate and methanolic ammonia,[11] the major product of the reaction being *N*,*N*-dibenzoyl-D-mannosylamine. In their studies on the syntheses of purine biosynthesis intermediates, Baddiley, Buchanan, Handschumacher, and Prescott[12] prepared *N*-chloroacetyl-β-D-glucopyranosylamine by the reaction of chloroacetyl chloride and 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine and subsequent *O*-deacetylation; the reactions of *N*-benzyloxycarbonylglycyl chloride or *N*-benzyloxycarbonylglycylethyl carbonate with 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine and with 2,3,5-tri *O*-benzoyl-D-ribofuranosylamine followed

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TABLE I

N-ACYLGLYCOSYLAMINES

Compound	Method[a]	Yield, %	M.P., °	$[\alpha]_D^b$	Formula	Calculated C	Calculated H	Calculated N	Found C	Found H	Found N
N-Acetyl-α-D-arabinopyranosylamine[c]	A	59	223–224	−69° (H_2O)	$C_7H_{13}NO_5$	43.99	6.80	7.33	43.65	6.69	7.44
N-Acetyl-β-D-xylopyranosylamine[d]	A	78	213–214	−2° (H_2O)	$C_7H_{13}NO_5$	43.99	6.80	7.33	43.53	6.87	6.94
	B	70	204–212								
N-Acetyl-β-D-glucopyranosylamine[e]	A	84	256	−20° (H_2O)	$C_8H_{15}NO_6$	43.43	6.84	6.33	43.39	6.82	5.94
	B	77	254–256	−16° (H_2O)							
N-Benzoyl-β-D-xylopyranosylamine	A	58	218–219	+10° (H_2O)	$C_{12}H_{15}NO_5$	56.91	5.97	5.53	57.01	5.84	5.08
N-Caprinoyl-β-D-glucopyranosylamine	B	55	254–256	+4° (Pyridine)	$C_{16}H_{31}NO_6$	57.62	9.39	4.21	57.63	9.57	4.09
N-Lauroyl-β-D-glucopyranosylamine	B	66	180–181	+3° (Pyridine)	$C_{18}H_{35}NO_6$	59.78	9.78	3.88	59.56	9.66	3.67
N-Myristoyl-β-D-glucopyranosylamine	B	68	176–178	−3° (Pyridine)	$C_{20}H_{39}NO_6$	61.65	10.11	3.61	61.62	10.19	3.47
N-Palmitoyl-β-D-glucopyranosylamine	B	80	175–177	+9° (Pyridine)	$C_{22}H_{43}NO_6$	63.26	10.39	3.36	63.16	10.20	3.43
N-Stearoyl-β-D-glucopyranosylamine	B	72	172–174	+4° (Pyridine)	$C_{24}H_{47}NO_6$	64.67	10.68	3.14	64.75	10.62	2.86

[a] A: *N*,*N*-Dimethylformamide method; B: Methanol method. [b] The temperature was 10° with the pentose derivatives and 15° with the glucose derivatives. [c] The L-isomer was reported[1] to show m.p. 222–224°, $[\alpha]_D^{20}$ +69.7° (H_2O). [d] The reported values[4] are m.p. 213–214°, $[\alpha]_D^{20}$ −0.7° (H_2O). [e] The reported values are m.p. 255°,[5] 257°,[3] 260°,[4] $[\alpha]_D$ −22.4°,[5] −22 → −23°,[3] −22.8°[4] (H_2O).

by partial hydrolyses yielded *N*-(*N'*-benzyloxycarbonylglycyl)-β-D-glucopyranosylamine[12] and the anomers of *N*-(*N'*-benzyloxycarbonylglycyl)-D-ribofuranosylamine,[13] respectively.

In the light of increasing importance of glycosylamines,[4,14] development of convenient and general methods selectively to *N*-monoacylate unsubstituted glycosylamines with various acyl groups appeared to be desirable. In the present work, two methods were studied on α-D-arabinopyranosylamine, β-D-xylopyranosylamine, and β-D-glucopyranosylamine, and their *N*-acetyl derivatives, *N*-benzoyl-β-D-xylopyranosylamine, and the *N*-acyl-β-D-glucopyranosylamines with a series of even-numbered fatty acids were prepared. All the compounds obtained in crystalline state are given with physical characteristics in Table I.

The two methods are extensions of the two methods reported recently for the selective *N*-acylation of D-glucosamine (2-amino-2-deoxy-D-glucose). Kuhn and Haber[15] prepared *N*-acetyl-β-D-glucosamine by the reaction of acetic anhydride and β-D-glucosamine in *N*,*N*-dimethylformamide at −15°, while Inouye, Onodera, Kitaoka, and Hirano[16] obtained *N*-acyl-D-glucosamines by the acylation with anhydrides of a series of fatty acids in methanolic supersaturated solution of D-glucosamine at room temperature or slightly higher temperatures.

In application of these methods to the *N*-acylation of unsubstituted glycosylamines, the *N*,*N*-dimethylformamide method was found to be more appropriate because glycosylamines are sparingly soluble in methanol and are more labile than glucosamine. The *N*-acylation of glycosylamines in the methanol method was therefore successful only with relatively more stable amines.

N-Acetylation of glycosylamines in *N*,*N*-dimethylformamide was carried out by suspending the glycosylamines in 15 to 25 molar equivalents of dimethylformamide at 0°, adding 1.5 equivalents of cold acetic anhydride with agitation and cooling, and shaking the mixtures for periods required for complete dissolution of the glycosylamines at room temperature. The periods ranged from a few minutes with β-D-glucopyranosylamine to about two hours

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with α-D-arabinopyranosylamine. Separation of crystalline *N*-acetylglycosylamines ensued usually immediately after the completion of the dissolution, and the crude yields were 60–80%. Use of larger amounts of acetic anhydride shortened the period before the dissolution but did not improve the yield.

The *N*-acetyl-D-xylosylamine and *N*-acetyl-D-glucosylamine thus obtained showed melting points and optical rotations essentially identical with the reported values for *N*-acetyl-β-D-xylopyranosylamine[4] and *N*-acetyl-β-D-glucopyranosylamine,[3–5] respectively. The infrared spectra potassium bromide of these compounds were identical with those of the compounds[17] prepared by *O*-deacetylation of *N*-acetyltri-*O*-acetyl-β-D-xylopyranosylamine and *N*-acetyltetra-*O*-acetyl-β-D-glucopyranosylamine. *N*-Acetyl-α-D-arabinopyranosylamine is a new compound but the L-enantiomorph is known.[1] The D-isomer here obtained had an identical melting point and an identical value of optical rotation with inversed sign as reported for the L-isomer. The infrared spectrum (potassium bromide) of the D-isomer was essentially identical with the spectrum[17] (potassium chloride) of the L-isomer. These results indicate that the anomeric structures of the original glycosylamines were retained during the *N*-acylation.

Acetylation of the *N*-acetylglycosylamines in pyridine and acetic anhydride gave good yields of the fully acetylated derivatives.

N-Benzoyl-β-D-xylopyranosylamine was prepared in 58% yield similarly by the *N*,*N*-dimethylformamide method. In this case the spontaneous separation of the *N*-benzoyl derivative did not follow the dissolution of β-D-xylopyranosylamine in the mixture of *N*,*N*-dimethylformamide and benzoic anhydride, and additions of ethanol and ether were required for the separation of the crystalline product.

The *N*-acetylation of unsubstituted glycosylamines in methanol was performed as follows: An amount of a glycosylamine was dissolved in 120 to 150 parts of methanol at 50° to make a saturated solution and to this was added with shaking 1.5 parts of acetic anhydride; the mixture was cooled immediately at 0° and kept there overnight. To isolate *N*-acetyl-glycosylamines it was usually necessary to concentrate the solutions to small volumes under reduced pressure before the spearation of crystals took place. The crude yields of the *N*-acetylglycosylamines in this method were similar or somewhat smaller than those in the *N*,*N*-dimethylformamide method. As previously stated, this method was successful only with more stable glycosylamines. *N*-Acetyl-β-D-xylopyranosylamine and *N*-acetyl-β-D-glucopyranosylamine were prepared by this method also. The products showed no depression in mixed melting point with the preparations by the *N*,*N*-dimethylformamide method. An attempt to *N*-acetylate α-D-arabinopyranosylamine gave only a resinous product.

A series of *N*-acyl-β-D-glucopyranosylamines with even-numbered fatty acids were prepared by the methanol method with the use of the respective acid anhydrides. *N*-Caprinoyl-, *N*-lauroyl-, *N*-myristoyl-, *N*-palmitoyl-, and *N*-stearoyl-β-D-glucopyranosylamines were obtained in crystalline form, while the *N*-butyryl, *N*-caproyl, and *N*-capryloyl derivatives were not crystalline.

(17) Kindly furnished by Dr. H. S. Isbell.

EXPERIMENTAL

Glycosylamines. Sugars were suspended in 2 to 2.5 parts of anhydrous methanol and into these suspensions was passed anhydrous ammonia at 0° with stirring until complete solutions were obtained. The solutions were kept at 0° for 1 to 4 weeks for satisfactory separation of the glycosylamines. After filtration, washing with methanol, and drying, the products were recrystallized from 100 parts of methanol or from a small volume of water by adding ethanol. The glycosylamines thus obtained and used for subsequent experiments were as follows: α-D-arabinopyranosylamine, a new amine obtained after recrystallizations from methanol in hygroscopic crystals, m.p. 70–85° (gas), $[\alpha]_D^{19}$ −52° (*c* 0.68, water). The L-isomer has been reported[1] to melt at 124–125°, $[\alpha]_D^{20}$ +86.3° (water). No satisfactory analyses were obtained from this preparation and apparently it was an impure product; β-D-xylopyranosylamine, m.p. 142–143°, $[\alpha]_D^{19}$ −18° (*c* 3.3, water). The reported values[4] are m.p. 128–129°, $[\alpha]_D^{20}$ −19.6°; β-D-glucopyranosylamine, m.p. 126–128°, $[\alpha]_D^{12}$ +22° (*c* 1.0, water). Reported, m.p. 127–128°,[18] 125–127°,[4] $[\alpha]_D$ +20.3°,[18] +20.8°,[4] +22.1°[19] (water).

N-Acetylation of glycosylamines in N,N-dimethylformamide. Suspensions of 0.02 mole of glycosylamines in 0.35 to 0.5 mole of dried *N*,*N*-dimethylformamide were cooled at 0°. To these was added 0.03 mole of acetic anhydride with shaking and cooling. The reaction mixtures were then shaken mechanically at room temperature. The glycosylamines went into solution after various periods of shaking; α-D-arabinopyranosylamine required about 2 hr., β-D-xylopyranosylamine about 1.5 hr., and β-D-glucopyranosylamine a few minutes. Separation of the crystalline *N*-acetylglycosylamines usually occurred rapidly after the dissolution of glycosylamines completed. The mixtures were kept overnight at 0°, and the crystals were collected by filtration and washed with small volumes of cold ethanol and ether, and recrystallized from methanol. The physical characteristics of the *N*-acetyl-glycosylamines thus prepared are given in Table I.

Experiments with D-xylopyranosylamine indicated that employment of larger amounts of acetic anhydride (up to 4.7 moles against 1 mole xylosylamine) shortened markedly the period (up to 20 min.) required for the dissolution of the amine, but the yield of the *N*-acetylated product was identical.

N-Benzoyl-β-D-xylopyranosylamine. Three grams of β-D-xylopyranosylamine were suspended in 18 ml. of *N*,*N*-dimethylformamide and cooled in an ice-bath. To this suspension was added 6.0 g. benzoic anhydride and the mixture was shaken at room temperature for 2 hr., by which time a complete solution had been obtained but no separation of crystals had occurred. The solution was allowed to stand at 0° overnight and to this was added 25 ml. ethanol

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and then 150 ml. ether to a turbidity which on agitation separated crystals. A small additional volume of ether was added and after standing overnight at 0° the crystals were collected by filtration and washed with small volumes of cold ethanol and ether. The yield was 3.0 g. (58%). Recrystallization from 20 ml. methanol gave needles, m.p. 218–219° dec., $[\alpha]_D^{10}$ +10° (*c* 2, water).

Acetylation of N-acetylglycosylamines in pyridine and acetic anhydride. One gram of an *N*-acetylglycosylamine was dissolved in 20–30 ml. pyridine and cooled to 0°. To this was added under cooling 5 ml. of cold acetic anhydride. The solution was kept at 0° for 1 hr. and then at room temperature overnight. It was poured into ice-water mixture, extracted with chloroform, and the chloroform extract washed with sodium bicarbonate solution, dilute hydrochloric acid, and water, dried over anhydrous sodium sulfate, and concentrated *in vacuo*. The fully acetylated products thus obtained and recrystallized from ethanol had the following physical constants: *N*-Acetyl-tri-*O*-acetyl-α-D-arabinopyranosylamine, m.p. 175–176°, $[\alpha]_D^{10}$ −90° (*c* 1.0, $CHCl_3$). The reported constants[1] for the L-isomer are m.p. 177–178°, $[\alpha]_D^{20}$ +89.6° ($CHCl_3$).

Anal. Calcd. for $C_{13}H_{19}NO_8$: C, 49.21; H, 6.04; N, 4.41. Found: C, 49.31; H, 6.14; N, 4.75.

N-Acetyl-tri-*O*-acetyl-β-D-xylopyranosylamine, m.p. 170–171°, $[\alpha]_D^{15}$ +28° (*c* 1.1, $CHCl_3$); in literature,[4] m.p. 172–173°, $[\alpha]_D^{20}$ +28.5° ($CHCl_3$).

N-Acetyl-tetra-*O*-acetyl-β-D-glucopyranosylamine, m.p. 163°, $[\alpha]_D^{15}$ +17° (*c* 1.0, $CHCl_3$); the reported values[4] are m.p. 163–164°, $[\alpha]_D^{20}$ +17.4° ($CHCl_3$).

N-Acylation of β-D-glucopyranosylamine in methanol. One gram (0.0056 mole) of β-D-glucopyranosylamine was dissolved in 120 ml. of methanol at 50°, and 0.0085 mole of acid anhydrides[16] was added with shaking to this solution followed by immediate cooling in an ice-box where it was allowed to stand overnight. *N*-Acetyl-β-D-glucopyranosylamine separated in crystalline state on concentration under reduced pressure to about 30 ml. and cooling. For *N*-butyryl, *N*-caproyl, and *N*-capryloyl derivatives, a small volume of ether was added after the concentration to separate precipitates which were hygroscopic and could not be crystallized. Additions of the anhydrides of capric, lauric, myristic, palmitic, and stearic acids were made in acetone or petroleum ether solutions; separation of the *N*-acyl-β-D-glucopyranosylamines with these acyl groups from the reaction solutions was spontaneous on cooling and needed no concentration. Recrystallization of the *N*-acyl compounds was effected by dissolving in 2 parts of water and adding 20 parts of ethanol or from methanol.

The *N*-acetyl-β-D-glucopyranosylamine prepared in the methanol method was identical with the product obtained in the *N,N*-dimethylformamide method as judged by mixed melting point and infrared spectra. Acetylation of these *N*-acetylated products in pyridine and acetic anhydride also gave an identical product, *N*-acetyl-tetra-*O*-acetyl-β-D-glucopyranosylamine.

The *N*-acetylation in methanol was attempted with α-D-arabinopyranosylamine and β-D-xylopyranosylamine by a similar procedure. The arabinosylamine gave only a resinous product while *N*-acetyl-β-D-xylopyranosylamine was obtained in crystalline state in a yield of 70%, m.p. 204–212° and mixed melting point with the product by the *N,N*-dimethylformamide method, 205–212°.

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[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES]

Reductive Dimerization in Formic Acid

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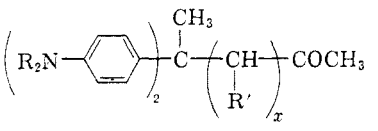
The formation of 1,1,3,3-tetrakis(*p*-dimethylaminophenyl)butane (VII) by the action of formic acid on 1,1-bis(*p*-dimethylaminophenyl)ethylene is reported.

In the course of a program to synthesize compounds similar to Amphenone B (I),[1] an attempt was made to prepare the tetramethylated Amphenone homolog II. Although the attempt was unsuccessful, some rather novel results were obtained.



I. R = H, x = 0
II. R = CH_3, x = 1, R′ = H
III. R = CH_3, x = 1, R′ = $COOC_2H_5$

The first step of the projected synthesis consisted in heating 1,1-bis(*p*-dimethylaminophenyl)-ethylene (IV) with acetoacetic ester in 98% formic acid as both solvent and catalyst. It was hoped that the ester III would be formed, which by decarbethoxylation could be converted into the ketone II. This reaction was modeled after a similar reaction by Fosse[2] in which acetoacetic ester and Michler's hydrol were condensed in the presence of acetic acid with the elimination of water to yield a benzhydrylacetoacetic ester. In the synthesis of the ester III the homolog of Michler's hydrol could not be used since all preparations leading to it resulted in the diphenylethylene IV.[3] [In this and all subsequent formulas R is $(CH_3)_2NC_6H_4$–.] This was thought to be of small consequence, however, since the same reactive

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