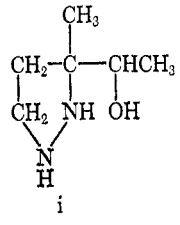
Anal. Calcd for $C_6H_{10}N_2O$: C, 57.12; H, 7.99. Found: C, 56.92; H, 8.22.

The phenylhydrazone melted at 119–120°. The semicarbazone did not have a sharp melting point, deforming and carmellizing at 230–240°.

Anal. Calcd for $C_6H_{11}N_5O$: C, 42.60; H, 6.54. Found: C, 42.49; H, 6.49.

A sample of the ketone in ethanol was hydrogenated with Raney nickel catalyst at 1000 psi and room temperature. Distillation gave a very viscous, colorless liquid assumed to be i, bp 89° (0.5 mm), $n^{29}D$ 1.4891.



i

Anal. Calcd for $C_6H_{14}N_2O$: C, 55.35; H, 10.84; N, 21.52. Found: C, 55.31; H, 10.27; N, 21.62.

C. With Cinnamaldehyde.—An ether–diazomethane solution, prepared as described before, was distilled into a solution of cinnamaldehyde in ether. The product solution was sealed in a precooled pressure bottle and let stand for 2 days. Removal of the ether gave a high yield of crude product, but an attempt to distil this material resulted in decomposition of a considerable amount of the desired product. The distillate crystallized to light yellow crystals. Three recrystallizations from ether–petroleum ether gave colorless crystals, mp 100–101° [lit.[9] light yellow crystals, mp 101° (with some indication of lower melting Δ^1 isomer), prepared from benzalacetone and diazomethane]. The infrared spectrum in CCl_4 showed bands at 3400 (NH), 1720 (C=O), 1670 (conjugated C=O), 1545 (N=N), and 1410 cm^{-1}, indicating a mixture of the 1-pyrazoline and 2-pyrazoline isomers.

Registry No.—**1a**, 23936-71-2; **2a**, 23936-72-3; **2b**, 23936-73-4; **3a**, 23936-74-5; **3b**, 23936-75-6; **4a**, 23936-76-7; **4b**, 23936-77-8; 3-acetyl-3-methyl-1-pyrazoline, 1567-95-9; 3-acetyl-3-methyl-1-pyrazoline phenylhydrazone, 23936-79-0; diazomethane, 334-88-3; semicarbazone of 3-acetyl-3-methyl-1-pyrazoline, 23936-81-4; i, 23936-80-3.

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N Acylation of D-Glucosamine by a New Method

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N-Acyl derivatives of D-glucosamine are of great interest in biochemical studies. Several methods for the preparation of N-acyl derivatives of D-glucosamine have been reported in the literature.[2-7] The latest method reported by Inouye, *et al.*,[8] for preparing N-acyl derivatives of D-glucosamine required the treatment of a supersaturated solution of D-glucosamine hydrochloride in methanol with sodium methoxide solution followed by removal of precipitated sodium chloride before any acid chloride or anhydride was added for the reaction.

We wish to report here a new method for N acylation of D-glucosamine, in which *p*-nitrophenyl esters were used as acylating agents.

Bodanszky[9] first reported that amino groups of tyrosine and serine with unprotected hydroxyl groups could be selectively acylated by *p*-nitrophenyl esters. We found this reagent to be very effective for the N acylation of amino sugars. This method was found to be simple, direct, and more convenient than all previously reported methods.

Three typical N-acyl derivatives of D-glucosamine were prepared by using *p*-nitrophenyl esters of acetic, benzoic, and stearic acids.

Analytical data and physical constants for the three N-acyl-D-glucosamines prepared are given in Table I. All the three compounds show absorption maxima at 510, 545, and 585 nm when submitted to the Morgan Elson color reaction as reported previously.[10]

Experimental Section

Melting points were taken in open capillaries and are uncorrected. Infrared spectra were determined with a Perkin-Elmer Model 521 infrared spectrophotometer, and absorption spectra in the visible range were obtained in Hilger Uvispeck spectrophotometer, Model H700. Optical rotations were measured with Hilger-Watts Model M-511 microptic photoelectric polarimeter.

Preparation of N-Acyl Derivatives of D-Glucosamine.—A representative experimental procedure is as follows. To a solution of *p*-nitrophenyl acetate (181 mg, 1 mmol) in 1.4 ml of freshly distilled dimethyl sulfoxide (DMSO) were added D-glucosamine hydrochloride (107 mg, 0.5 mmol) and triethylamine (0.07 ml, approx 0.5 mmol). Higher proportions of DMSO were required to dissolve *p*-nitrophenyl benzoate and *p*-nitrophenyl stearate. The mixture was stirred for 1 hr at room temperature, and, after standing for 4 days at 20°, the yellow mixture was diluted with 15 vol of dry methylene chloride (*ca.* ten times the volume of DMSO used). Excess of *p*-nitrophenyl acetate and triethylamine hydrochloride remained in solution and N-acetyl-D-glucosamine gradually separated out. The mixture was centrifuged after being allowed to stand for 2 hr, and the residue was washed twice with methylene chloride and three times with dry ether and finally dried over concentrated sulfuric acid. The yield was almsost quantitative. The crude material was crystallized from methanol by addition of ether to incipient turbidity.

Preparation of *p*-Nitrophenyl Stearate.—Stearic acid (2.3 g, 0.008 mol) was refluxed with thionyl chloride (3 ml, 0.04 mol) on water bath for 4 hr and kept overnight at 20°. Excess thionyl chloride was removed *in vacuo* at 100°. To the reaction product in the flask, dry pyridine (5 ml) was added while the flask was cooled in ice, and then, to this mixture, *p*-nitrophenol (2 g, 0.015 mol) in dry pyridine (10 ml) was added. Some solid appeared in the flask which was dissolved by heating to 50°. The reaction mixture was kept at 20° for 40 hr and then poured in crushed ice. The mixture was acidified to congo red with H_2SO_4, cooled in ice

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TABLE I
N-ACYL DERIVATIVES OF D-GLUCOSAMINE

Derivative	Mp, °C	[α]D	Yield, %	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N	Ir (secondary amide), cm⁻¹ >C=O	Ir (secondary amide), cm⁻¹ >NH
N-Acetyl	206	+39.5[a]	q	$C_8H_{15}O_6N$	43.43	6.84	6.33	43.20	6.80	6.27	1625	3320
N-Benzoyl	198–200	+35.0[a]	q	$C_{13}H_{17}O_6N$	55.12	6.05	4.95	54.90	5.95	4.84	1630	3295
N-Stearoyl[b]	208	+24.3[c]	80	$C_{24}H_{47}O_6N$	64.68	10.63	3.14	64.53	10.50	2.95	1640	3300

[a] After 24 hr (c 2, water). [b] Inouye, *et al.*,[8] reported [α]D +78°. [c] After 24 hr (c 1, pyridine) (q stands for almost quantitative).

for 1 hr, and filtered. The product was washed with water and dried, yield 2.4 g. The crude product was dissolved in ethanol (100 ml) by boiling, decolorized with charcoal, and filtered hot. On cooling *p*-nitrophenylstearate crystallized in needles, mp 68.8°. *Anal.* Calcd for $C_{24}H_{39}O_4N$: C, 71.0; H, 9.69; N, 3.40. Found: C, 71.07; H, 9.69; N, 3.45.

p-Nitrophenyl acetate and *p*-nitrophenyl benzoate were prepared as reported previously.[11,12]

Registry No.—D-Glucosamine, 3416-24-8; *p*-nitrophenyl stearate, 14617-86-8; Table I (derivatives)—N-acetyl, 7512-17-6; N-benzoyl, 655-42-5; N-stearoyl, 24299-14-7.

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Reduction of N-Chlorosulfonyl β-Lactams to β-Lactams with Sodium Sulfite

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Chlorosulfonyl isocyanate (CSI) has been shown to react with a variety of olefinic substances to give N-chlorosulfonyl β-lactams.[1-4] These compounds have been reduced by a variety of methods to β-lactams, the overall reaction serving as an important route to such compounds.

In general, the published procedures for the reduction step, (a) benzenethiol–pyridine in acetone at −30°,[5,6] (b) potassium iodide in aqueous sodium hydroxide,[1,5,6] (c) Raney nickel in ethanol,[5,6] aqueous hydrolysis,[5] and (d) 4 *N* KOH in acetone[7] or saturated methanolic KOH,[4] have suffered from variable yields because of reaction conditions under which some N-chlorosulfonyl β-lactams are not stable (methods b to d) and difficulties in separation of the desired lactams from biproducts (method a).[6]

In connection with a problem in which we required large quantities of seveal β-lactams, we decided to investigate the reduction of N-chlorosulfonyl β-lactams with an inorganic reducing agent such as sodium sulfite. This compound was an obvious choice since it has been known for some time that sodium sulfite is capable of reducing aliphatic and aromatic sulfonyl chlorides to the corresponding sulfinic acids.[8] In the case of N-chlorosulfonyl β-lactams such a reduction would give the N-sulfinic acid which could readily lose sulfur dioxide to afford the β-lactam.

Experimentally it was found that such reductions occurred within a few minutes and in high yield when a solution of the N-chlorosulfonyl β-lactam in ether or other suitable organic solvent was stirred with a 25% aqueous sodium sulfite solution at room temperature. The pH of the aqueous phase was kept slightly basic by addition of 10% KOH solution as the reduction proceeded. The advantages of the method are simplicity of the reaction and isolation procedures, easy adaptation to large-scale reactions, mild reaction conditions, and high yield of pure product. The reduction can be run at 0°, thereby allowing reduction of heat sensitive N-chlorosulfonyl lactams.

When pure N-chlorosulfonyl β-lactams were employed, near-quantitative yields of β-lactams could be isolated. In cases in which the N-chlorosulfonyl β-lactams were thermally unstable and difficult to isolate, *e.g.*, those derived from isoprene or butadiene,[2] the reduction was carried out at 0° on the crude CSI–olefin reaction product. The yields of β-lactam based on CSI were of the order of 70% (see Table I).

The structures assigned to the new lactams (from methylene cyclohexane and 1,3-cyclooctadiene) were those expected on the basis of a two-step reaction mechanism for the cycloaddition reaction;[1] they are, in addition, supported by spectroscopic and analytical data (see Experimental Section).

Experimental Section

Reactions of CSI with Olefins.—Known N-chlorosulfonyl β-lactams were prepared according to published procedures (see Table I).

CSI and 1,3-Cyclooctadiene.—Equimolar amounts of CSI and diene were heated overnight in benzene at 50°. The crude product obtained after washing the reaction mixture with water and evaporating the benzene layer was extracted twice with pentane to remove unreacted diene. The oily material so obtained (80%) was pure by thin layer chromatography (tlc). The infrared spectrum ($CHCl_3$) showed a strong band at 5.52 μ. Nmr peaks were at δ 1.2–2.5 (8 H), 3.4–4.0 (1 H), 5.1–5.5 (1 H), and 5.6–6.2 (2 H).

CSI and Methylenecyclohexane.—CSI (3.5 g) was added dropwise to 2.4 g of methylenecyclohexane in 10 ml of ether at 10°. The reaction mixture became semisolid with fine needles. The product was filtered and recrystallized from ether, yield 5.1 g (96%), mp 88–90°. The infrared spectrum showed the

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