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.

Acknowledgments.—Our thanks are due to Mrs. C. Dutt of Indian Association for the Cultivation of Science, Calcutta, for the microanalysis and to Mr. S. Bhattacharya of Indian Statistical Institute, Calcutta, for technical assistance.

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

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Received February 17, 1970

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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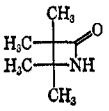
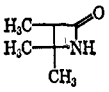
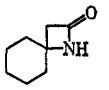
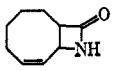
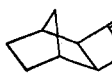
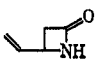
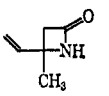
TABLE I

REDUCTION OF N-CHLOROSULFONYL β-LACTAMS WITH Na_2SO_3

N-Chlorosulfonyl β-lactam prepared from	β-Lactam	Yield, %	Ref
2,3-Dimethyl-2-butene (a)		92	5
2-Methyl-2-butene (b)		98	5
Methylenecyclohexane (c)		98	
1,3-Cyclooctadiene (d)		97	
Norbornene (e)		77	3
1,3-Butadiene[a] (f)		72	2
Isoprene[a] (g)		68	2

[a] N-Chlorosulfonyl lactam was not isolated.

lactam band at 5.53 μ. Nmr absorption was at δ 1.0–2.8 (10 H) and 3.05 (s, 2 H).

Anal. Calcd for $C_8H_{12}ClNO_3S$: C, 40.4; H, 5.05; N, 5.90. Found: C, 40.17; H, 5.05; N, 5.82.

Reaction of N-Chlorosulfonyl β-Lactams with Na_2SO_3. General Procedure.—A solution of N-chlorosulfonyl β-lactam dissolved in ether was added slowly to a stirred mixture of about two parts 25% aqueous sodium sulfite and one part ether. The aqueous phase was kept slightly basic by addition of 10% KOH solution as the reduction proceeded. The reaction course could easily be followed by thin layer chromatography in which the product had a considerably smaller R_f value than the starting material. At the end of the reaction (usually less than 15 min) the ether layer was separated and dried and the solvent evaporated. The products were of greater than 95% purity as determined by nmr. The reduction could be carried out either at 25 or 0°.

1-Aza-2-keto[6.2.0]bicyclodec-8-ene.—N-Chlorosulfonyl β-lactam (2.25 g) was dissolved in 15 ml of ether and added to a mixture of 5 ml of ether and 10 ml of 25% aqueous sodium sulfite. The aqueous phase was kept between pH 7 and 8 by addition of 10% KOH solution. After 15 min tlc showed the absence of starting material and the formation of only one ether soluble product. The ether layer was separated and dried and the solvent was evaporated to yield 1.32 g (97%) of solid. Recrystallization from ethanol gave colorless granules: mp 100–101°; ir ($CHCl_3$) 5.71 μ; nmr ($CDCl_3$) δ 1.2–2.4 (8 H), 3.2–3.6 (1 H), 4.4–4.7 (1 H), 4.2–5.0 (2 H), and 6.8–7.2 (1 H).

Anal. Calcd for $C_9H_{13}NO$: C, 71.5; H, 8.60; N, 9.26. Found: C, 71.12; H, 8.62; N, 9.10.

1-Azaspiro[3.5]nonan-2-one was prepared as above in 98% yield: colorless oil; bp 123° (4.2 mm); ir ($CHCl_3$) 5.72 μ; nmr ($CDCl_3$) δ 1.3–2.0 (10 H), 2.61 (d, J = 1.5 cps, 2 H, collapses to singlet on addition of D_2O), 7.3–8.0 (broad singlet 1 H).

Anal. Calcd for $C_8H_{13}NO$: C, 69.00; H, 9.34; N, 10.07. Found: C, 69.33; H, 9.39; N, 10.00.

Registry No.—Table I—lactam a, 17060-95-6; b, 24571-92-4; c, 24571-93-5; d, 24571-94-6; e, 24571-95-7; f, 22937-11-7; g, 20012-93-5; sodium sulfite, 7757-83-7; 1-azaspiro[3.5]nonan-2-one, 24571-98-0; 1-aza-2-keto[6.2.0]bicyclodec-8-ene, 24571-99-1.

Acknowledgments.—Financial support of this project by the National Research Council of Canada is gratefully acknowledged.

Evaluation of the σ* Parameter for Halodinitromethyl Groups

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Received October 31, 1969

Hine and Bailey[1] have determined the Taft σ* parameter for a number of polynitroalkyl groups and noted that the value of σ* for the trinitromethyl group, 4.54, is the largest recorded for an electrically neutral substituent. In connection with other studies, we required the σ* values for fluoro-, chloro-, and bromodinitromethyl substituents. We have evaluated the σ* parameter for these substituents by measuring the rates of reaction of the corresponding 4-halo-4,4-dinitrobutyric acids with diphenyldiazomethane in ethanol at 30°. These data are summarized in Table I.

TABLE I

RATE OF REACTION OF 4-Z-4,4-DINITROBUTYRIC ACID WITH DIPHENYLDIAZOMETHANE IN ETHANOL AT 30°

Z	k, M^{-1} min^{-1}
F	3.56 ± 0.04
Cl	3.36 ± 0.16[a]
Br	3.18 ± 0.03

[a] 2.97 ± 0.03 at 25°.

From these specific rate constants and the equation[1]

$$\log k = -0.105 + 1.174\,\sigma^*$$

we obtained σ* values for the 3-halo-3,3-dinitropropyl functions (Table II). Though the error in the value

TABLE II

TAFT σ* PARAMETERS

R	σ*
$FC(NO_2)_2CH_2CH_2$	0.559 ± 0.005
$ClC(NO_2)_2CH_2CH_2$[a]	0.537 ± 0.017
$BrC(NO_2)_2CH_2CH_2$	0.517 ± 0.004
$FC(NO_2)_2$[b]	4.4
$ClC(NO_2)_2$[b]	4.2
$BrC(NO_2)_2$[b]	4.1

[a] σ* = 0.538 ± 0.005 from 25° data. [b] By multiplying σ* for $ZC(NO_2)_2CH_2CH_2$ by (2.8)[2].

of k at 30° for 4-chloro-4,4-dinitrobutyric acid is unexplainedly about four times larger than that for the fluoro and bromo acids, measurements of the specific rate at 25° afforded a much more precise value of the rate constant for the chloro acid (Table I). Calculating σ* for the 3-chloro-3,3-dinitropropyl function from the 25° data gives a value which is essentially identical with the one obtained from the 30° rate data.

Experimental Section

Preparation of 4-Halo-4,4-dinitrobutyric Acids.—The fluoro acid, prepared by hydrolyzing the corresponding methyl ester,[2] was obtained as colorless needles, mp 37–38°.

Chlorination and bromination of potassium methyl 4,4-dinitroburyrate in pentane afforded methyl 4-chloro- and methyl 4-

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