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ACETYLATION OF OXAZOLIDINES WITH KETENE

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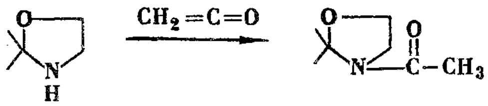
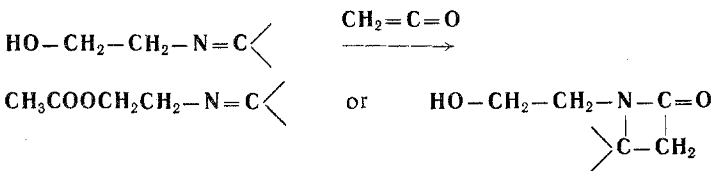
For the first time oxazolidines are acetylated with ketene, at the nitrogen atom, to give a number of hitherto unknown N-acetyloxazolidines.

Previous authors have not investigated direct acetylation of oxazolidines at the nitrogen atom. It has been reported that carbon suboxide reacts with a number of cyclic imines to give good yields of the corresponding malonylamides [1]. The present authors also extended that reaction to oxazolidines [2].

The reaction of oxazolidines with ketene was investigated in the present work. The reaction of ketene with heterocyclic and acyclic forms of oxazolidines was not excluded, since the latter are labile, and prone to such tautomerism. In the first case formation of N-acetyloxazolidine was to be expected, and in the second, of esters of β-lactams.





It is shown that ketene reacts with oxazolidines in the first way only. The following is the evidence for formation of N-acetyloxazolidines: a) ketene reacts readily with ethanolamines at the amino group, the hydroxyl group acetylating under comparatively drastic conditions, most frequently in the presence of catalysts [3], b) Schiff's bases react with ketene only at temperatures of the order of 200°. The IR spectra of the compounds synthesized exhibited distinct absorption bands corresponding to valence vibrations of the group $>N-C\genfrac{}{}{0pt}{}{\nearrow O}{\searrow}$ (1650—1490 cm^{-1}). Valence vibrations, characteristic of the ester group, in the region 1760-1740 cm^{-1}, were absent.

N-acetyloxazolidines are rather stable compounds, confirming a previously expressed opinion [4] that a substituent at the nitrogen atom stabilizes the heterocyclic system of the oxazolidine molecule.

By reacting ketene with a number of oxazolidines, N-acetyloxazolidines of the following general formula were synthesized:

R and $R'=CH_3$ and CH_3 (I), CH_3 and C_2H_5 (II), $CH_2\genfrac{}{}{0pt}{}{\diagup CH_2CH_2}{\diagdown CH_2CH_2}$ (III), C_6H_5 and H (IV), CH_3 and C_6H_5 (V), C_2H_5 and C_6H_5 (VI), o-HOC_6H_4 and H (VII), o-$CH_3OC_6H_4$ and H (VIII), m-$NO_2C_6H_4$ and H (IX), p-$NO_2C_6H_4$ and H (X), p-$NO_2C_6H_4$ and CH_3 (XI).

Experimental

Ketene was prepared by pyrolysis of acetone [5]. The oxazolidines were as follows: 2, 2-dimethyloxazolidine bp 32-34° (10 mm), 2-methyl-2-ethyloxazolidine bp 48° (14 mm), 2-cyclohexanooxazolidine bp 80-81° (9 mm), 2-phenyloxazolidine bp 126-127° (7-8 mm), 2-methyl-2-phenyloxazolidine bp 129-130° (7 mm), 2-ethyl-2-phenyloxazolidine bp 112-113° (4 mm), 2-(o-hydroxyphenylene) oxazolidine bp 154-155° (3 mm), 2-(o-methoxyphenylene) oxazolidine bp 147° (15 mm), and 2-(m-nitrophenylene) oxazolidine, 2-(p-nitrophenylene) oxazolidine, 2-methyl-2-(p-nitrophenylene) oxazolidine. They were oily liquids which decomposed on distillation, and were prepared by Cope's method [6], as modified by the present authors [7].

Compounds I-XI were prepared by the typical method. Two cases, preparation of liquid and solid products, are given here by way of example.

Preparation of IV. The acetylation was run in a three-necked flask fitted with reflux condenser, thermometer, and bubbler for introducing the ketene gas. 25 g (~ 0.17 mole) freshly-distilled 2-phenyloxazolidine, 50 ml dry toluene were put in the flask, and a steady stream of ketene passed into the mixture. 20 min after reaction began, the temperature of the mixture was raised to 70°. Ketene was passed till the temperature dropped to 45° (e.g., using 150% of the theoretical ketene). The mixture was then left overnight, the toluene distilled off under reduced pressure (140-160 mm) and the residue fractionated. Compound IV was a liquid which readily turned yellow, bp 160-161° (2 mm), yield 29.5 g(92%).

Properties of N-Acetyloxazolidines Synthesized

Compound No.	Mp, or bp, °C (pressure, mm)	d_4^{20}	n_D^{20}	Formula	Found				Calculated				Yield, %
					C, %	H, %	N, %	M	C, %	H, %	N, %	M	
I	88—89 (6)	0.9780	1.4580	$C_7H_{13}O_2N$	58.93	10.12	9.95	—	58.7	9.65	9.79	—	60
II	50—52 (17)	1.0391	1.4420	$C_8H_{15}O_2N$	61.35	9.36	9.04	—	61.2	9.55	8.92	—	62
III	59—60 (Mp)	—	—	$C_{10}H_{17}O_2N$	65.68	9.58	7.94	186	65.6	9.29	7.65	183	75
IV	160—161 (2)	1.1550	1.5439	$C_{11}H_{12}O_2N$	68.98	7.15	7.49	—	69.1	6.81	7.33	—	92
V	161—163 (6)	1.0721	1.5233	$C_{12}H_{15}O_2N$	76.31	7.49	6.71	—	76.1	7.31	6.82	—	82
VI	79—80 (Mp)	—	—	$C_{13}H_{17}O_2N$	71.68	7.94	6.18	214	71.3	7.76	6.38	219	65
VII	136—137 (Mp)	—	—	$C_{11}H_{13}O_3N$	63.42	6.03	6.71	—	63.7	6.28	8.76	207	72
VIII	83—84 (Mp)	—	—	$C_{12}H_{15}O_3N$	65.28	6.41	6.36	229	65.2	6.79	6.33	221	86
IX	86—87 (Mp)	—	—	$C_{11}H_{12}O_4N$	55.74	5.32	11.71	240	55.9	5.08	11.83	236	60
X	86—87 (Mp)	—	—	$C_{11}H_{12}O_4N$	55.81	4.92	12.03	237	55.9	5.08	11.83	236	68
XI	79—80 (Mp)	—	—	$C_{12}H_{14}O_4N$	57.51	5.23	11.39	244	57.6	5.6	11.2	250	76

Note. Compounds IX-XI are readily crystallized from petrol ether + carbon tetrachloride. The other compounds are crystallized from benzene, or ether + methanol (10 : 1).

Preparation of IX. A slight excess of ketene was passed into a solution of 15 g (0.084 mole) 2-(m-nitrophenylene) oxazolidine in 70 ml dry toluene. After the completion of reaction, the toluene was distilled off and the residue (a syrupy mass) left in a refrigerator for 3-4 days. The mass crystallized when rubbed vigorously with a glass rod. The crystals were washed with cold ether, and recrystallized from benzene. Compound IX was a white crystalline substance, mp 86-87°, readily soluble in alcohol and acetone, insoluble in water. Yield 16.4% (60%).

The solubilities of compounds I-XI (Table) were similar.

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