were heated at 100–200° for 24 hours with litharge, potassium carbonate, sodium hydride, tetraisopropyl titanate and 2,5-dichlorobenzenesulfonic acid. Lactones and cyclic ureas were heated at 150–260° with water and sodium hydride for a similar period.

Lactam VI polymerized so quickly when heated to 200° that melting could not be completed before the polymer congealed. Attempts to moderate the reaction with milder catalysts (see below) or by conducting it in solution in ethyl benzoate, γ-butyrolactone, pyrrolidone or 5,5-dimethylpyrrolidone,[1] gave no improvement in yield or molecular weight. Lactam V polymerized at a much slower rate and addition of N-acetylcaprolactam was beneficial. Lactone IV polymerized at about the same rate, confirming earlier work.[6,7] Lactone XI polymerized slowly to give a low molecular weight, solvent-sensitive polymer. The polyurethan obtained from XII was also sensitive to solvent and of low molecular weight.

Because the reaction of VI with sodium hydride proceeded too rapidly for convenient control, a search was made for other catalysts. The following were ineffective (at 200° for 24 hours): water, ε-aminocaproic acid, sodium or potassium carbonate, sodium acetate, boric acid, sodium phosphite, litharge, antimony trioxide, tetraisopropyl titanate, γ-butyrolactone, toluenesulfonic acid and sodium cyanide. All salts were tested with and without a trace of water. Phosphoric acid gave a very small yield of polymer. At the boiling point of the lactam, sodium phenoxide and carbonate were still ineffective.

Poly-3-cyclohexanecarboxamide was soluble in *m*-cresol, sulfuric acid, trifluoroacetic acid, 90 and 99% formic acids, 60% trichloroethane–40% formic acid and 60% chloroform–40% formic acid. The 4-isomer dissolved in sulfuric acid, 99% formic acid, and in the mixtures of the latter with chloroform and trichloroethane. It was insoluble in *m*-cresol, trifluoroacetic acid and 90% formic acid.

Both polymers depolymerized to the corresponding lactams when heated with a flame, the 1,3-isomer at lower temperatures.

Because of the possibility of isomerization during polymerization, these polymers may be mixtures of *cis* and *trans* forms.

Chelates.—A relationship between ease of formation of chelate compounds and of bicyclic organic compounds has been noted and discussed.[61–63] In agreement with this concept, the feasibility of forming cyclic and bicyclic ureas from diamines could be assessed by seeing whether or not they formed chelates with metal ions.

The diamine was added to an aqueous solution of cupric acetate. The appearance of an intense violet color was taken as an indication of chelate formation. The following gave positive tests: ethylenediamine, trimethylenediamine, *cis*-1,3-diaminocyclohexane, *cis*- and *trans*-1,4-diaminocyclohexane and 1,8-diamino-*p*-menthane gave negative tests. This order is in good accord with the observed tendencies of these diamines to form cyclic ureas. This test should also apply to aminocyclohexanols.

For the best results a metal atom should have the same stereochemistry as the carbon atom to which it will correspond. However, we have used copper (square planar) to correspond to carbonyl carbon (trigonal planar) because of easily observed color changes on chelation.

(61) S. J. Angyal and D. J. McHugh, *J. Chem. Soc.*, 1423 (1957).
(62) P. Lions and K. V. Martin, THIS JOURNAL, **79**, 1572 (1957).
(63) Z. Foldi, T. Foldi and A. Foldi, *Chemistry & Industry*, 1297 (1955); 466 (1957).

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[CONTRIBUTION FROM THE PIONEERING RESEARCH DIVISION, TEXTILE FIBERS DEPARTMENT, E. I. DU PONT DE NEMOURS AND CO., INC.]

Hydrolysis Rates and Mechanisms of Cyclic Monomers

BY H. K. HALL, JR., M. K. BRANDT AND R. M. MASON

RECEIVED JUNE 30, 1958

The rates of hydrolysis of a number of imides, N-acyllactams and lactones were determined. The data were combined with information in the literature and compared with the polymerizability of the cyclic compounds. No correlation was observed, hence hydrolysis rates do not measure ring strain. The slow step in the hydrolysis is the addition of OH^- to the ring, leaving the ring unbroken. The enhanced reactivities of lactones over esters was ascribed to repulsion of the lone pair electrons on oxygen in the latter toward the hydroxyl ion. This postulate uses the transition state proposed by Ballard and Bamford, which is also consistent with substituent effects in the 5-membered rings. The 6-membered compounds showed the usual rate depression caused by 1,3- interaction with methyl substituents.

Carothers[1] suggested that polymerizability and rates of hydrolysis of cyclic monomers should run parallel.[1] It is the purpose of this article to examine this suggestion more closely.

The results of the investigation are given in Table I and are summarized in Table II.

Relationship of Hydrolysis Rate to Polymerizability.—Rings of extremely high reactivity to alkali relative to the acyclic derivative are prone to polymerize. These include ethylene oxalate,[1] δ-valerolactone,[1] propiolactam,[2] 2,5-piperazinedione,[3] lactide[4] and glycolide.[4] To this extent Carothers' proposal is valid.

Other rings show no correlation with polymerizability. For example, 2-piperidone hydrolyzes faster than 2-pyrrolidone, yet the polymerizabilities are markedly in the reverse order.[5] Propiolactone polymerizes readily and γ-butyrolactone does not, yet the two lactones hydrolyze at comparable rates.[6] The suggestion of Carothers is therefore not generally valid.

Polymerizability of a cyclic compound is an indication of strain in the ring[7] and since the hydrolysis rate is not determined by strain in the ring, it follows that the ring is not broken in the rate-determining step; the latter must consist of addition of OH^- to the ring, in agreement with Bender's results for open-chain compounds.[7c]

Reactivity of Cyclic Compounds Relative to Acyclics.—Table III makes clear that only lactones (and possibly cyclic carbonates)[8] exhibit a large

(1) "Collected Papers of W. H. Carothers," Interscience Publishers, Inc., New York, N. Y., 1940, p. 148.
(2) R. W. Holley and A. D. Holley, THIS JOURNAL, **71**, 2129 (1949).
(3) W. Kuhn, C. C. Molster and K. Freudenberg, *Ber.*, **65**, 1179 (1932).
(4) "Intern. Crit. Tables," Vol. VII, p. 135.
(5) H. K. Hall, Jr., THIS JOURNAL, **81**, 6412 (1959).
(6) F. A. Long and M. Purchase, *ibid.*, **72**, 3267 (1950).
(7) (a) G. E. Wheland, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 366; (b) F. S. Dainton and K. J. Ivin, *Quart. Revs.*, **12**, 82 (1958); (c) M. L. Bender, THIS JOURNAL, **73**, 1626 (1951), and later papers.
(8) Sh. Sarel and A. Pothoryles, *Compt. rend.*, **245**, 2321 (1957).

TABLE I

RATE DATA

Acyl derivative	Concn. × 10³	$k_1 \times 10^3$	k_2	Method
Acetylcaprolactam	1.49	2.86	1.9	Cap.
	1.70	2.99	1.8	Cond.
	2.99	6.11	2.1	Cap.
	4.04	7.08	1.8	Cond.
	5.42	9.80	1.8	Pot.
	7.51	13.3	1.8	Cond.
	10.7	17.3	1.6	Pot.
	15.6	23.2	1.5	Pot.
	20.3	39.4	1.9	Pot.
			1.80 Av.	
Acetyl-5-methyl-caprolactam	10.3	13.3	1.3	Pot.
	17.6	21.1	1.2	Pot.
	26.1	34.7	1.3	Pot.
	33.8	54.8	1.6	Pot.
			1.35 Av.	
N-Acetyl-2-piperidone	1.57	3.04	1.9	Cap.
	3.15	6.31	2.0	Cap.
	4.07	7.13	1.8	Cond.
	5.85	13.1	1.6	Pot.
	9.12	16.3	1.8	Cond.
	9.84	15.6	1.6	Pot.
	19.2	33.1	1.7	Pot.
	28.0	41.7	1.5	Pot.
	36.3	50.6	1.4	Pot.
			1.70 Av.	
N-Acetyl-2-pyrrolidone	1.73	4.22	2.4	Cap.
	2.82	6.27	2.2	Cond.
	3.48	8.63	2.5	Cap.
	3.96	9.71	2.5	Cond.
	4.87	11.8	2.4	Pot.
	10.7	24.1	2.3	Cond.
	21.3	46.6	2.2	Pot.
			2.36 Av.	
N-Isobutyryl-pyrrolidone	1.45	5.15	3.6	Cap.
	2.77	8.25	3.0	Cap.
	3.97	9.87	2.5	Cap.
	5.09	12.7	2.5	Cap.
	14.9	28.1	1.9	Pot.
			2.7 Av.	
N-Benzoylpyrrolidone	2.92	9.46	3.2	Cond.
	5.82	16.0	2.8	Pot.
			3.0 Av.	
N-Benzoylcaprolactam	2.54	2.76	1.1	Cond.
	4.55	4.18	0.90	Cond.
			1.0 Av.	
N-Acetyloxazolidone	1.76	5.13	2.9	Cap.
	3.52	11.0	3.1	Cap.
	6.81	18.3	2.7	Cond.
	9.23	24.7	2.7	Pot.
	10.7	33.0	3.1	Cond.
	17.0	52.5	3.1	Cond.
	17.6	45.7	2.6	Pot.
			2.89 Av.	
N-Methyldiacetamide	2.12	3.72	1.8	Cap.
	4.16	7.75	1.9	Cap.
	4.25	9.63	2.3	Cap.
	6.29	8.77	1.4	Pot.
	7.14	9.28	1.3	Pot.
	19.2	21.3	1.1	Pot.
	19.3	24.4	1.3	Pot.
	32.6	40.4	1.2	Pot.
			1.54 Av.	
N-Acetyltrimethylene urethan	1.77	3.90	2.2	Cap.
	4.86	8.43	1.7	Cap.
	6.22	10.0	1.6	Cap.
	7.50	10.8	1.4	Cap.
	16.3	20.7	1.3	Pot.
	39.9	46.8	1.2	Pot.
			1.57 Av.	
N-Methylglutarimide	1.71	3.90	2.3	Cap.
	6.03	10.7	1.8	Cap.
	7.23	14.1	2.0	Cap.
	9.40	17.5	1.9	Cap.
	10.35	16.2	1.6	Pot.
	19.75	31.3	1.6	Pot.
	28.3	42.7	1.5	Pot.
			1.81 Av.	
N-Methylsuccinimide	70.7	9.71	0.14	Pot.
	73.7	12.7	.17	Cap.
	111	15.4	.14	Cap.
	154	20.3	.13	Cap.
	174	25.2	.15	Pot.
			0.146 Av. (0.753)[c]	
N-Acetylethyleneurea	23.5	2.61	0.13	Cap.
	45.0	6.21	.14	Cap.
	56.5	4.57	.081	Cap.
	60.5	4.86	.080	Pot.
	68.8	4.64	.068	Cap.
	137.3	8.88	.065	Pot.
			.094 Av.	
N-Acetyl-2-aza-bicyclo[2:2:2] octan-3-one-(IV)	1.36	2.36	1.7	Cap.
	3.60	3.40	0.94	Cap.
	6.00	5.25	.88	Cap.
	6.21	5.31	.86	Pot.
	10.0	8.75	.88	Cap.
	12.9	11.6	.90	Cap.
	19.8	18.5	.94	Pot.
	41.6	38.4	.92	Pot.
			0.90 Av.	
N-Acetyl-6-aza-bicyclo[3:2:1] octan-7-one-(III)	1.08	5.40	5.0	Cap.
	1.98	6.71	3.4	Cap.
	2.85	8.53	3.0	Pot.
	2.86	9.47	3.3	Cap.
	4.41	14.3	3.2	Cap.
	5.41	21.8	4.0	Cap.
	7.47	24.2	3.2	Pot.
	13.2	42.4	3.2	Pot.
			3.3 Av.	
γ-Butyrolactone	5.32	5.41	1.02	Pot.
	10.1	7.91	0.78	Pot.
	16.1	13.2	.82	Pot.
	31.4	23.2	.74	Pot.
	34.7	24.0	.69[a]	Cond.
			0.81 Av. (1.11[a])	

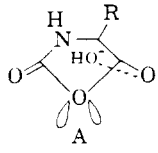
TABLE I (*Continued*)

Acyl derivative	Concn. × 10³	k_1 × 10³	k_2	Method
γ-Valerolactone	2.85	8.90	0.31(0.467[d])	Cond.
δ-Valerolactone	2.39	32.7	13.7	Pot.
	4.78	66.3	13.9	Pot.
			13.8 Av.	
ε-Caprolactone	8.31	6.61	0.80	Pot.
	21.9	16.5	.76	Pot.
	38.7	29.1	.75	Pot.
			0.77 Av.	
Ethylene bromohydrin			.35	Pot.
			.35	Pot.
			0.35 Av.(0.45–0.50[b])	
N-Ethoxycarbonyl-pyrrolidone	13.5	3.65	0.27	Pot.
	34.7	11.3	.33	Pot.
			0.30 Av.	
N-Methanesulfonyl-pyrrolidone	20.2	9.07	0.45	Pot.
	38.5	16.7	.43	Pot.
			0.44 Av.	
6-Oxabicyclo[3:2:1]-octan-7-one (I)	9.14	2.98	0.33	Pot.
	27.5	10.4	.38	Pot.
	62.6	22.9	.37	Pot.
			0.36 Av.	
2-Oxabicyclo[2:2:2]-octan-3-one (II)	38.8	1.09	0.028	Pot.
	85.6	2.15	.025	Pot.
			0.027 Av.	

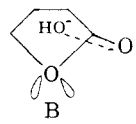
[a] D. S. Hegan and J. H. Wolfenden, *J. Chem. Soc.*, 508 (1939), give an extrapolated value of 1.11 l. mole^{-1} sec.$^{-1}$; M. Gordon, Thesis, Manchester, 1950, gives a lower value for butyrolactone at 0° (0.124 against 0.196). [b] Ethylene bromohydrin: C. L. McCabe and J. C. Warner, THIS JOURNAL, **70**, 4031 (1948), give an extrapolated value of 0.45–0.50 l. mole^{-1} sec.$^{-1}$. [c] N-Methylsuccinimide: Miolati and Longo, ref. *g*, Table III. These authors report their rate constants as Ak_2, where A is the initial concentration of both imide and base. For N-methylsuccinimide we find k_2 = 0.753 l. mole^{-1} sec.$^{-1}$ by dividing by 0.005 × 60. The data of other investigators (S. S. G. Sircar, *J. Chem. Soc.*, 602, 1252 (1927); W. Hückel and H. Muller, *Ber.*, **64B**, 1981 (1931)) are to be multiplied by 10 and divided by the above factor. See also Sircar, *J. Chem. Soc.*, 898 (1928). [d] γ-Valerolactone: Hegan and Wolfenden, ref. *a*, give 0.467 l. mole^{-1} sec.$^{-1}$. Again, Gordon's value (ref. *a*) is slightly lower at 0°, 0.0719 *vs.* 0.0824.

rate enhancement over their acyclic analogs (*cf.* Table III of ref. 16). Other cyclic compounds react at comparable rates to the open chain forms. The reason appears to be the following.

Ballard and Bamford[9] suggest that N-carboanhydrides are attacked by hydroxide ion via the transition state shown in A.

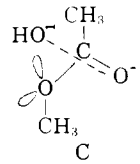


A

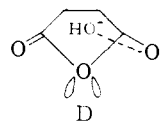


B

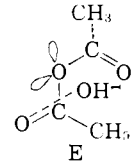
Applying this concept to lactones B, we see that hydroxyl ion, when attacking the *cis*-lactone, avoids unfavorable electrostatic repulsion from the lone pair atom dipole of oxygen.[10-12] In open-chain *trans* esters C this interaction cannot be avoided, so esters react abnormally slowly. Anhydrides react equally quickly in the cyclic (D) or acyclic (E)



C



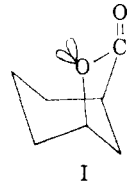
D



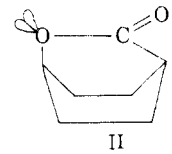
E

compounds, for the lone pair electrons cannot shield both carbonyl groups in the latter simultaneously. The same factor may well account for the depressed reactivity of dimethyl phosphate anion relative to ethylenephosphate anion.[13]

The above postulate of rearward attack on ester carbonyl groups by hydroxide ion is supported by the results for 6-oxabicyclo[3:2:1]octan-7-one (I) and for 2-oxabicyclo[2:2:2]octan-3-one (II). The conformational formulas show that rearward attack as described above is possible for I over the 5-membered ring, and the rate constant approximates those for other 5-membered lactones. Rearward attack is impossible for II, however, and the rate constant is drastically lowered to a value near that of an aliphatic ester. In the transition state for hydrolysis of this hindered lactone, the hydroxyl ion attacks the *p*-orbital of the carbonyl group, with



I



II

TABLE II

SUMMARY OF RATE DATA

Acyllactam	k_{ring}	k_{acr}
N-Acetyl-2-pyrrolidone	0.64	1.72
N-Acetyl-2-piperidone	0.77	0.93
N-Acetylcaprolactam	1.39	.41
N-Acetyl-5-methylcaprolactam	1.00	.35
N-Isobutyrylpyrrolidone	0.85	1.85
N-Benzoylpyrrolidone	2.7	0.67
N-Benzoylcaprolactam	0.39	.61
N-Acetylimidazolidone	0.004>	.094
N-Acetyloxazolidone	1.25	1.64
N-Acetyltetrahydroöxazinone	0.33	1.24
N-Methyldiacetamide	..	1.54
N-Methylsuccinimide	0.15	..
N-Methylglutarimide	1.81	..
N-Acetyl-6-azabicyclo[3:2:1]octan-7-one (I)	3.33	0.15>
N-Acetyl-2-azabicyclo[2:2:2]octan-3-one (II)	0.31	0.59
6-Oxabicyclo[3:2:1]octan-7-one (III)	.36	..
2-Oxabicyclo[2:2:2]octan-3-one (IV)	.027	..
N-Methanesulfonylpyrrolidone	.44	..
N-Ethoxycarbonylpyrrolidone	.30	..

(9) D. G. H. Ballard and C. H. Bamford, *J. Chem. Soc.*, 355 (1958).

(10) C. A. Coulson, "Valence," Clarendon Press, London, 1952, pp. 207–211.

(11) T. Nash, *J. Appl. Chem.*, **6**, 300 (1956).

(12) W. J. Orville-Thomas, *Chem. Revs.*, **57**, 1193 (1957).

(13) J. Kumamoto, J. R. Cox, Jr., and F. H. Westheimer, THIS JOURNAL, **78**, 1858 (1956).

TABLE III
HYDROLYSIS RATES OF CYCLIC COMPOUNDS

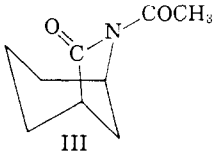
Reaction	Rate factor[a]	Temp., °C.	Acyclic rate constant	5-Ring rate constant	6-Ring rate constant	7-Ring rate constant
Lactone + OH^{-}[b]	10^{-2}	0	0.04	15	550	25.5
Lactam + OH^{-}[c]	10^{-4}	75	1.92	1.8	8.7	0.84
N-Methyllactam + OH^{-}[c]	10^{-4}	75	1.92	0.700	4.78	...
N-Acetyllactam + OH^{-}[d]	1	25	1.54	1.02	0.77	1.39
Imides + OH^{-}[e,f]	1	25	0.92	3.16	0.63	...
N-Methylimides + OH^{-}[d,g]	1	25	1.54	0.15	1.81	...
Anhydrides + H_2O[h]	10^{-3}	20	1.90	1.83	2.00	...
Anhydrides + OH^{-}[h]	10^{3}	0	14.3	5.54	9.10	...
N-Acetylurethanes + OH^{-}[d]	1	25	...	1.24	0.314	...

[a] Multiply the rate constant given in table by this factor to get actual value in l. $mole^{-1}$ $sec.^{-1}$. [b] R. Huisgen, *et al.*, *Angew. Chem.*, 69, 345 (1957); C. W. Matuszak and H. Schechter, Abstracts of 132nd A.C.S. Meeting, New York, N. Y., September 1957, p. 12P. [c] M. Gordon, Thesis, Manchester, 1950. [d] Present work. [e] Corrected for ionization of the imide. [f] J. T. Edward and K. A. Terry, *J. Chem. Soc.*, 3527 (1957); J. T. Edward and S. Nielsen, *ibid.*, 5080 (1957) [g] A Miolati, *Atti della reale Accad nazionale Lincei*, [5] **3**, 515 (1894); A Miolati and E. Longo, *ibid.*, [5] **3**, 597 (1896); [h] J. Koskikallio, *Ann. Acad. Sci. Fennicae, Series A*, No. 57 (1954).

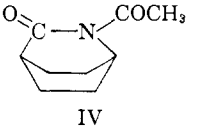
a consequent electrostatic repulsion from the atomic dipole of the O atom.

In the hydrolysis of these lactones by water,[14] where electrostatic considerations are minimized because the attacking reagent is now uncharged, the lactones react at comparable rates. However this reaction may have a quite different mechanism, and more work on this problem would be helpful.

The N-acetyl lactams present a different picture. N-Acetyl-6-azabicyclo[3:2:1]-octan-7-one (III), undergoes ring cleavage ten times as rapidly as N-acetyl-2-azabicyclo[2:2:2]-octan-3-one (IV).



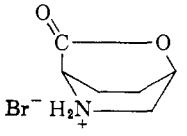
III



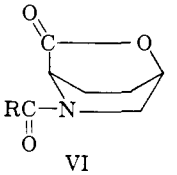
IV

Because the lone pair electrons on the N atom strongly interact with the carbonyl group, the necessity for rearward attack by hydroxyl is apparently not as stringent as for the lactones. Thus IV undergoes ring cleavage at a rate comparable to other imides. It will be recalled that both of these lactams undergo sodium-catalyzed polymerization with facility, wherein the key step is the attack of a lactam anion on the N-acyl lactam. Anionic reagents, therefore, can attack both these lactams and their N-acyl derivatives at appreciable rates. The facile ring cleavage of III probably is caused by inhibition of the N—C=O interaction by the bridged structure.

It is of interest that the bicyclic lactone V hydrolyzes quickly in water, whereas the N-acyl lactone VI is much more stable.[15] A direct field effect of the positive pole on the carbonyl group may be responsible.



V

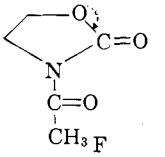


VI

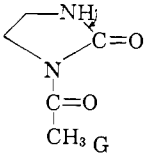
(14) R. R. Grewe, C. Heinke and C. Sommer, *Chem. Ber.*, **89**, 1978 (1956).

(15) B. Witkop and C. B. Foltz, THIS JOURNAL, **79**, 194 (1957).

Effect of Hetero Atoms in the Ring.—Replacement of methylene by oxygen adjacent to the carbonyl group has negligible effect on the rates. There is little interaction of the type shown in F.



F



G

Replacement by NH, however, brings about strong interaction as in G and the ring cleavage rate is markedly depressed.

Relative Reactivities of 5- and 6-Membered Rings.—Table III shows that there is no great difference in the hydrolysis rates of 5- and 6-membered compounds except for lactones[16] and carbonates.[8] The appreciable rate factor in the lactone group appears to be associated with the presence of a single trigonal or sp^2 atom in the ring. The Brown–Brewster–Schechter rule[16] is therefore of limited validity.

It can be noted incidentally that imides and N-acetyl-lactams are far more reactive toward anionic attack than lactams, a result required by the previously proposed mechanism for alkali-catalyzed polymerization.

Effects of Ring Substituents.—The effects of ring substituents were not studied in this work but an examination of the literature led to the conclusions summarized in Table V.

These results are entirely consistent with the transition state configuration given by Ballard and Bamford[9] for the 5-membered rings. For the 6-membered rings a destabilizing effect of alkyl groups in the 3-position is clearly evident. This is well established as a conformational effect in the cyclohexane series.[17–19]

Effect of N-Substituents.—The fact that N-methanesulfonylpyrrolidone hydrolyzes at a rate comparable to the N-acetyl or N-benzoyl derivatives strongly supports the contention that addition

(16) H. C. Brown, J. H. Brewster and H. Schechter, *ibid.*, **76**, 467 (1954).

(17) O. H. Wheeler and J. Z. Zabicky, *Chemistry & Industry*, 1388 (1956).

(18) O. H. Wheeler, THIS JOURNAL, **79**, 4191 (1957).

(19) W. Klyne, *Experientia*, **12**, 119 (1956).

TABLE IV

SOURCES OF IMIDES, ACYL LACTAMS AND LACTONES FOR KINETICS STUDIES

Compound	Preparation	Properties	Anal.	Literature ref.
N-Acetylpyrrolidone	Pyrrolidone, acetic anhyd.	B.p. 99° (4 mm.), d^{25}_4 1.1420, $n^{25}D$ 1.4828	Calcd. for $C_6H_9O_2N$: C, 56.7; H, 7.1; N, 11.0. Found: C, 56.5; H, 6.8; N, 10.8	W. Reppe, *et al.*, *Ann.*, **596**, 201 (1955), give b.p. 118° (20 mm.)
N-Acetyl-δ-valerolactam	δ-Valerolactam, acetic anhyd.	B.p. 72° (0.10 mm.), $n^{25}D$ 1.4894	Calcd. for $C_7H_{11}O_2N$: C, 59.6; H, 7.9; N, 9.9. Found: C, 59.7; H, 8.2; N, 9.8	C. Schotten, *Ber.*, **21**, 2242 (1888), gives b.p. 238°
N-Acetylcaprolactam	Caprolactam, acetic anhyd.	B.p. 104–106° (3 mm.), $n^{25}D$ 1.4875	.....	R. E. Benson and T. L. Cairns, THIS JOURNAL, **70**, 2115 (1948), give b.p. 135° (27 mm.), $n^{25}D$ 1.4885
Diacetamide	Acetamide, isopropenyl acetate	M.p. 81–82°	.....	W. Hentschel, *Ber.*, **23**, 2395 (1890), gives m.p. 78°
N-Methyldiacetamide	N-Methylacetamide, isopropenyl acetate	B.p. 71° (7 mm.), $n^{25}D$ 1.4532	Calcd. for $C_5H_9O_2N$: N, 12.2. Found: N, 12.2	A. W. Hofmann, *Ber.*, **14**, 2731 (1881), gives b.p. 192°
N-Methyldiformamide	Courtesy of Dr. W. R. Sorenson	B.p. 67° (7 mm.), $n^{25}D$ 1.4571	Calcd. for $C_3H_5O_2N$: N, 16.1 Found: N, 16.1	J. D. Ray, H. O. Kammen, L. H. Piette and R. A. Ogg, Jr., *J. Org. Chem.*, **21**, 1052 (1956) give b.p. 183°
N-Methylsuccinimide	Succinic anhydride, methylamine, distil	M.p. 65.5–67.5°	.....	J. Bredt and W. Boedddinghaus, *Ann.*, **251**, 320 (1889), give m.p. 66°
N-Methylglutarimide	Glutaric anhydride, methylamine, distil	B.p. 124° (14 mm.), $n^{25}D$ 1.4944; crystd. on standing, m.p., *ca.* 30°	.....	L. Irrera, *Gazz. chim. ital.*, **65**, 464 (1935), gives b.p. 129° (15 mm.)
N-Benzoylpyrrolidone	Pyrrolidone, benzoyl chloride, dimethylformamide	M.p. 85°	.....	Reppe, *et al.*, above, give m.p. 89°
N-Benzoyl-δ-valerolactam	δ-Valerolactam, benzoyl chloride, dimethylformamide	M.p. 130.6–133.3°, sol. 0.04 g./l. water	.....	T. B. Graves, THIS JOURNAL, **46**, 1469 (1924), gives m.p. 121°
N-Benzoylcaprolactam	Caprolactam, benzoyl chloride, dimethylformamide	M.p. 67.0–69.5°, sol. 1.48 g./l. water	.....	L. Ruzicka, *Helv. Chim. Acta*, **4**, 478 (1921), gives m.p. 46°
N-Phenylcarbaminopyrrolidone	Pyrrolidone, phenyl isocyanate, sodium hydride	M.p. 94°, sol. 0.62 g./l. water	.....	W. Reppe, *et al*, above, give m.p. 98°
N-Acetyloxazolidone	Oxazolidone, acetic anhyd.	B.p. 96° (0.25 mm.), m.p. 66.0–67.3°	.....	A. H. Homeyer, U. S. Patent 2,399,118, gives m.p. 69–70°
N-Acetyltetrahydroöxazinone	Tetrahydroöxazinone, isopropenyl acetate	B.p. 108° (1 mm.), $n^{25}D$ 1.4872	Calcd. for $C_6H_9O_3N$: C, 50.3; H, 6.3; N, 9.8. Found: C, 50.3; H, 6.0; N, 9.7	.....
N-Acetylethyleneurea	Ethyleneurea, acetic anhydride	M.p. 171.5–173.0°	Calcd. for $C_5H_8O_2N_2$: C, 46.9; H, 6.3; N, 21.9. Found: C, 46.9; H, 6.1; N, 21.5	.....
N-Isobutyrylpyrrolidone	Pyrrolidone, isobutyric anhyd.	B.p. 107° (7 mm.), m.p. 34.5–35.0°	Calcd. for $C_8H_{13}O_2N$: C, 61.9; H, 8.4; N, 9.0. Found: C, 61.9; H, 8.3; N, 8.9	.....
N-Acetylthiopyrrolidone	Thiopyrrolidone, isopropenyl acetate	B.p. 90° (1.5 mm.)	Calcd. for C_6H_9ONS: C, 50.3; H, 6.3; N, 9.8. Found: C, 50.6; H, 6.2; N, 9.8	.....
N-Acetyl-6-azabicyclo[3:2:1]octan-7-one	6-Azabicyclo[3:2:1]octan-7-one, acetic anhydride	B.p. 92° (0.6 mm.), $n^{25}D$ 1.5012	Calcd. for $C_9H_{13}O_2N$: C, 64.7; H, 7.8; N, 8.4. Found: C, 64.7; H, 7.8; N, 8.4	.....

TABLE IV (*Continued*)

Compound	Preparation	Properties	Anal.	Literature ref.
N-Acetyl-2-azabicyclo[2.2.2]octan-3-one	2-Azabicyclo[2.2.2]octan-3-one, acetic anhydride	B.p. 97° (1.3 mm.), m.p. 48.5–49.0°	Calcd. for $C_9H_{13}O_2N$: C, 64.7; H, 7.8; N, 8.4. Found: C, 64.5; H, 7.5; N, 8.4	E. Ferber and H. Brueckner, *Ber.*, **76**, 1019 (1943), give m.p. 48–50°
N-Acetylsuccinimide	Succinimide, acetic anhyd.	B.p. 103° (0.25 mm.)	.....	J. Tafel and M. Stern, *ibid.*, **33**, 2225 (1900), give b.p. 167° (9.5 mm.)
N,N'-Diacetylpiperazinedione	Piperazinedione, isopropenyl acetate	M.p. 100.5–101.0°	Calcd. for $C_8H_{10}O_4N_2$: C, 48.5; H, 5.1; N, 14.1. Found: C, 48.3; H, 5.0; N, 13.8.	A. P. N. Franchimont and H. Friedmann, *Rec. trav. chim.*, **27** (1908), give m.p. 102°
N-Acetyl-5-methylcaprolactam	5-Methylcaprolactam, acetic anhyd.	B.p. 80° (0.25 mm.), $n^{25}D$ 1.4827	Calcd. for $C_9H_{15}O_2N$: C, 63.9; H, 8.9; N, 8.3. Found: C, 63.1; H, 8.9; N, 8.2	.....
N-Benzoylsuccinimide	Courtesy of Dr. M. Baevsky	M.p. 129–130°	.....	A. W. Titherley, *J. Chem. Soc.*, **85**, 1685 (1904), gives m.p. 129–130°
γ-Butyrolactone	General Aniline and Film	.....	.....	.....
δ-Valerolactone	Aldrich Chemical Co. Dist. polymer from Pb_3O_4 at 3 mm. to depolymerize, redist.	B.p. 84° (3.5 mm.)	.....	E. Hollo, *Ber.*, **61**, 895 (1928) gives b.p. 116–118° (25 mm.).
ε-Caprolactone	Union Carbide and Carbon	B p. 105–109° (3.5 mm.)	.....	F. J. van Natta, J. W. Hill and W. H. Carothers, THIS JOURNAL, **56**, 455 (1934), give b.p. 98–99° (2 mm.).

TABLE V

Five-rings	Reference
	*a*
	*b*
	*c*
Six-rings	
	*d*
	*d*
	*c*
	*d*

[a] Summarized by "Intern. Crit. Tables," Vol. VII, p. 134. [b] S. S. G. Sircar, *J. Chem. Soc.*, 1252 (1927). [c] S. S. G. Sircar, *ibid.*, 898 (1928). [d] L. E. Hinkel, E. E. Ayling, J. F. J. Dippy and T. H. Angel, *ibid.*, 814 (1931); E. G. Meek, J. H. Turnbull and W. Wilson, *ibid.*, 2891 (1953). [e] S. S. G. Sircar, *ibid.*, 600 (1927).

of the hydroxyl ion to the ring carbonyl is the slow step of the hydrolysis. If the ring were breaking in the slow step, the methanesulfonyl group would stabilize the incipient N^- anion much better than the other acyl groups (*cf.* the acidity of sulfonamides relative to carboxamides). This near equality is not a polar effect offset by a steric one, for N-methylpyrrolidone hydrolyzes at a rate similar to that of pyrrolidone, so steric effects are minor.

Substituents on N or C always decrease polymerizability. They may or may not decrease hydrolysis rate. Again a lack of parallelism between the two properties is evident.

Rates of Acyl Cleavage.—The imides and acyllactams studied in the present work are about as reactive toward alkali as phenyl esters[20] or as N-benzoylimidazole.[21] They might therefore be useful acylating agents except for the possibility of alternate modes of reaction[22] (see below).

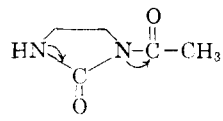
Acetyl and isobutyryl were cleaved faster than benzoyl, primarily for electronic reasons, from pyrrolidone.

In N-acetylimidazolidone, the interactions shown depress both rate constants. Neighboring oxygen, in N-acetyloxazolidone, is ineffective in this regard.

(20) E. Tommila and C. N. Hinshelwood, *J. Chem. Soc.*, 1801 (1938).

(21) H. A. Staab, W. Otting and A. Ueberle, *Z. Elektrochem.*, **61**, 1000 (1957).

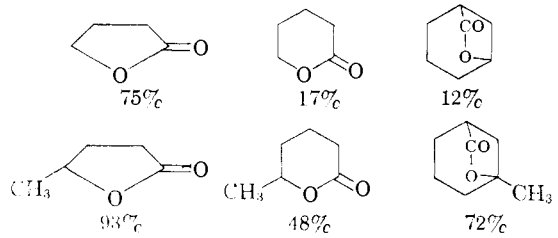
(22) P. Schlack, U. S. Patent 2,303,177 (1943).



Ring *vs.* Acyl Cleavage in Synthesis.—The question of whether the acyl group or the ring will be cleaved by alkali is of interest in synthetic work. Examination of the literature revealed that N-acetyllactams usually undergo deacetylation[26-30] whereas N-benzoyllactams are described as undergoing ring cleavage.[30-33]

Our results indicate that the two reactions usually proceed at comparable rates. However, N-benzoyl-2-piperidone was not studied in this work owing to its low solubility. Since the literature results refer to 6-membered lactams, the ring cleavage rate may be higher for these N-benzoyl derivatives than for the 5- and 7-membered compounds.

Another Criterion for Polymerizability.—As recognized by Linstead and Rydon,[36] the *equilibrium* constants for the hydrolysis of lactones by *water*[34-39] offer promise as measures of polymerizability. The percentage lactone at equilibrium has been shown to be



The influence of substitution and of ring size on these quantities parallels those on polymerizability.

Acknowledgments.—We are indebted to Mr. J. L. Sease for excellent experimental assistance, to Dr. P. W. Morgan for unfailing encouragement, and to Professors E. M. Kosower and H. Kwart for helpful discussion.

Experimental

Preparation of Materials.—The preparation of most of the compounds studied followed conventional methods which need not be described in detail. Pertinent information is given in Table IV.[40]

Many attempts to prepare N-methane- or N-benzenesulfonyllactams from the acid chloride and lactam directly, either with or without pyridine, 2,6-lutidine or dimethylformamide, failed. Heating benzenesulfonamide with γ-butyrolactone also gave no N-sulfonyllactam.

N-Methanesulfonyl- and N-Ethoxycarbonyllactams.—The lactam, 1.0 mole, *p*-toluenesulfonic acid (200.0 g., 1.05 moles) and 50 ml. of water were heated under reflux by an oil-bath at 130° for 48 hours. While the mixture was still warm, the water was removed under aspirator vacuum, whereupon the residue crystallized. It was ground up in a mortar, extracted with ethyl acetate, filtered and dried to give the hydrotosylate salt of the amino acid.

4-Aminobutyric acid hydrotosylate: 269.2 g. (97.8%), m.p. 137–138°. *Anal.* Calcd. for $C_{11}H_{17}O_5NS$: C, 48.0; H, 6.2. Found: C, 48.4; H, 6.1.

5-Aminovaleric acid hydrotosylate: 284.0 g. (98.2%), m.p. 145–146°. *Anal.* Calcd. for $C_{12}H_{19}O_5NS$: C, 49.8; H, 6.6. Found: C, 49.8; H, 6.4.

6-Aminocaproic acid hydrotosylate: 300.6 g. (99.1%), m.p. 160–161°. *Anal.* Calcd. for $C_{13}H_{21}O_5NS$: C, 51.5; H, 7.0. Found: C, 51.6; H, 7.1.

Acylations of these amino acid salts were carried out by a standard procedure. The amino acid hydrotosylate, 0.25 mole, and 10.0 g. (0.25 mole) of sodium hydroxide were dissolved in 350 ml. of water. To this were added simultaneously over a 30-minute period with stirring and cooling the acid chloride, 0.25 mole, and a solution of 20.0 g. (0.50 mole) of sodium hydroxide in 100 ml. of water. The mixture then was stirred for 15 minutes more and acidified with 50 ml. of 12 *N* hydrochloric acid. Precipitation occurred only with derivatives of 6-aminocaproic acid. The solutions were evaporated to dryness on the steam-bath under aspirator vacuum. The precipitate was extracted thoroughly with hot chloroform or with acetone. Filtration, followed by evaporation, gave the crude acylamino acid. This was distilled in a Claisen flask at 0.5 mm.[41]

The N-ethoxycarbonyl derivatives distilled smoothly to give good yields of crude yellow liquids contaminated with considerable quantities of water. They were taken up in chloroform, dried with $MgSO_4$, and redistilled in a spinning band column at a 10:1 or 20:1 reflux ratio. The pyrrolidone derivative was obtained as 10.45 g. of colorless liquid, b.p. 111–113° (0.60 mm.), $n^{25}D$ 1.4718.

Anal. Calcd. for $C_7H_{11}O_3N$: N, 8.9. Found: N, 8.8.

The piperidone and caprolactam derivatives were obtained only in impure form by this procedure.

The N-methanesulfonyl derivatives distilled with considerable decomposition at 0.5–1.0 mm. and, in the case of the pyrrolidone derivative, with a mildly exothermic reaction half-way through the distillation. Crude yellow solids or dark liquids, contaminated with considerable amounts of water were taken up in chloroform, dried with $MgSO_4$, and evaporated.

N-Methanesulfonyl-2-pyrrolidone.—The crude material, 10 g., was recrystallized from benzene–ethyl acetate (9:1), then from benzene to give 5.3 g. of glittering white crystals, m.p. 113–114°.

Anal. Calcd. for $C_5H_9O_3NS$: C, 36.8; H, 5.6. Found: C, 37.2, 36.7, 37.2, 37.7; H, 5.9, 5.7, 5.6, 5.9.

The piperidone and caprolactam derivatives were not obtained in pure form by this route. Probably the milder cyclization conditions employed by Poduska and Rudinger[42] would give better results.

Kinetics Methods—Potentiometric.—This method consists of allowing a minute quantity of alkali to react with a 10–20-fold excess of lactam in dilute water solution, and following the rate of the reaction by the change of *p*H with time.[43,44] Under these circumstances the rate of reaction is given by

(23) Ethyl acetate is about ten times as reactive as ethyl isobutyrate toward alkali, and about twenty times as reactive as ethyl benzoate (National Bureau of Standards Circular No. 510, pp. 100, 106).

(24) Acetamide is about seventy times as reactive as benzamide (I. Meloche and K. J. Laidler, THIS JOURNAL, **73**, 1712 (1951)).

(25) Diacetamide hydrolyzes much faster than dibenzamide (A. W. Titherley and L. Stubbs, *J. Chem. Soc.*, **105**, 306 (1914)).

(26) W. A. Noyes and R. S. Potter, THIS JOURNAL, **34**, 1072 (1912); **36**, 125 (1914); **37**, 195 (1915).

(27) J. Bredt, J. Houben and P. Levy, *Ber.*, **35**, 1291 (1902).

(28) W. H. Mills and J. B. Whitworth, *J. Chem. Soc.*, 2738 (1927).

(29) R. G. Petrova, L. N. Akimova and N. I. Gavrilov, *J. Gen. Chem. U.S.S.R.* (*Eng. trans.*), **24**, 2201 (1954).

(30) A. R. Battersby and J. C. Robinson, *J. Chem. Soc.*, 2076 (1956), observed comparable amounts of acyl and ring cleavage for both N-alkanoyl- and N-benzoylpyrrolidones.

(31) E. Bamberger and S. Williamson, *Ber.*, **27**, 1458 (1894).

(32) W. Hückel and F. Stefp, *Ann.*, **453**, 163 (1927).

(33) B. M. Regan and F. N. Hayes, THIS JOURNAL, **78**, 639 (1956).

(34) R. P. Linstead, *J. Chem. Soc.*, 115 (1932).

(35) E. J. Boorman and R. P. Linstead, *ibid.*, 577 (1933).

(36) R. P. Linstead and H. N. Rydon, *ibid.*, 1995 (1934).

(37) R. P. Linstead and H. N. Rydon, *ibid.*, 258 (1935).

(38) F. D. Coffin and F. A. Long, THIS JOURNAL, **74**, 5767 (1952).

(39) R. Grewe, A. Heinke and C. Sommer, *Chem. Ber.*, **89**, 1978 (1956).

(40) The use of isopropenyl acetate to acylate lactams is described by H. J. Hagemeyer, Jr., U. S. Patent 2,656,360 (1953).

(41) C. S. Marvel and W. W. Moyer, Jr., *J. Org. Chem.*, **22**, 1065 (1957).

(42) K. Poduska and J. Rudinger, *Coll. Czech. Chem. Comm.*, **22**, 1283 (1957).

(43) H. F. Walton and A. A. Schilt, THIS JOURNAL, **74**, 4995 (1952).

(44) A. Disteche and M. Dubuisson, *Rev. Sci. Instr.*, **25**, 869 (1951).

$$-d(OH^-)/dt = k_2(OH^-)(\text{acyllactam}) = k_1(OH^-)$$

Then

$$2.30 \log \frac{(OH^-)_0}{(OH^-)_t} = k_1 t$$

and

$$2.30\ pH_0 - 2.30\ pH_t = k_1 t$$

Therefore, a plot of pH against time will be linear with a slope of $-0.43k_1$. In this expression autoprotolysis of the water has been ignored. If this is taken into account, it can be shown

$$-p\text{H} + \frac{10^{-14}}{4.6\,(OH^-)^2} = \frac{k_1 t}{2.303} + C$$

At pH 8 or above the correction term is 0.005 pH unit or less, hence negligible. At pH 7 it amounts to 1/4.6 or about 0.25 pH unit.

Protolysis of the carboxylate ion cannot proceed to more than 0.5% at the pH ranges under study here.

Experimentally, a 500-ml. flask fitted with openings for glass and calomel electrodes (Beckman), for a stirrer and for introduction of the alkali was used. A solution 0.005–0.05 N in acyllactam was made up using boiled distilled water. With stirring was added 0.1 N sodium hydroxide solution from a small pipet until the pH was 10–11. Readings were taken until the pH became 8 or lower.

Except for four very electrophilic compounds, the spontaneous hydrolysis of the imides was negligible. These were N-methyldiformamide, N-acetylsuccinimide, N-benzoylsuccinimide and N,N'-diacetyl-2,5-piperazinedione. No change of initial pH (6–7) was noted until the alkali was added. Also, Hentschel[45] has shown that diacetamide hydrolyzes with a half-life of 17 hours in water at 66°.

As expected, plots of pH against time were linear for some compounds. For others, appreciable curvature occurred after >95% reaction (1.7 pH units), the reaction proceeding more slowly toward the end. This effect did not appear to be caused by traces of reactive impurities. Thus, after one run with N-acetylpyrrolidone had been followed to pH 7, more alkali was added and a new run was begun. The same curvature was observed. Also a vapor-phase chromatogram failed to detect impurities in the N-acetylpyrrolidone. Pyrrolidone itself does not hydrolyze under these conditions. Similarly, the curvature in the case of γ-butyrolactone was not affected by added alcohol or sodium acetate. Even ethylene bromohydrin exhibited this behavior. These deviations have not been observed by previous workers. Their methods (conductance, titration) focused attention on the first 10–80% of the reaction, whereas the present method follows the reaction to 99.9% completion. Our other two methods (see below) failed to detect this curvature except in the extreme case of N-methylsuccinimide, where the reaction is definitely of higher order in alkali.

The origin of this behavior is unknown. It might be due to higher order reactions[46] or to a trace of carbon dioxide in the water. In the calculations, the initial linear portion of the curve was used to calculate the rate constant.

There is also a downward trend of the bimolecular rate constant with increasing concentration in some cases. The significance of this fact is not known.

Capacitance and conductimetric methods were performed according to methods described in the literature.[47,48] As before, a small amount of hydroxyl ion was allowed to react with excess acyllactam. First-order kinetics, with no drifts, were observed.

Product Analysis.—A dilute aqueous solution of 4–8 millimoles of acyllactam, 0.01–0.05 M, was titrated slowly with 0.1 N sodium hydroxide solution, pH being maintained at 10–11, until exactly one equivalent had been added. The solution was poured into an evaporating dish, evaporated to near dryness at room temperature in a good hood, and made up to 25.00 ml. with distilled water. The lactam concentration was determined from a standard infrared calibration curve of an aqueous solution as follows.

(45) W. Hentschel, *Ber.*, **23**, 2395 (1890).

(46) S. S. Biechler and R. W. Taft, Jr., THIS JOURNAL, **79**, 4927 (1957), and references therein.

(47) P. J. Elving and J. Lakritz, *ibid.*, **77**, 3217 (1955).

(48) D. S. Hegen and J. H. Wolfenden, *J. Chem. Soc.*, 508 (1939); F. A. Long and M. Purchase, THIS JOURNAL, **72**, 3267 (1950).

TABLE VI

Compound	Infrared absorption wave length, μ
Pyrrolidone	7.76
2-Piperidone	7.88
Caprolactam	8.37
5-Methylcaprolactam	8.01
Oxazolidone	7.97
Trimethyleneurethan	8.90
Ethyleneurea	7.85
2-Azabicyclo[2:2:2]octan-3-one	9.05
6-Azabicyclo[3:2:1]octan-7-one	8.66

The analyses were performed using a Perkin–Elmer model 21 spectrophotometer, using the following specifications: slit width 30 μ at wave length 2.00 μ (slit program 985), response setting 2, automatic suppression 4, speed 3, gain setting 4 (this was always checked for optimum setting at 6.5 μ). Spectra were performed in CaF_2 cells from 2.00–10.00 μ) distilled water being used in the reference cell. Standard solutions of the products of acyl cleavage, *i.e.*, lactams, urethans or ureas, were made up in 1 and 10% solutions. It was *necessary* to perform the analysis at the same time as the standardization. The number of milliequivalents of lactam, etc., were calculated from the formulas, where

M = molecular weight of lactam
P = weight/volume percentage of standard soln.
A = background absorption
A_{max} = absorption at the selected maximum
K = absorption constant for the sample
L = volume of reaction solution

$$K = \frac{A_{max} - A_{background}}{P}(\text{from data of std. soln.})$$

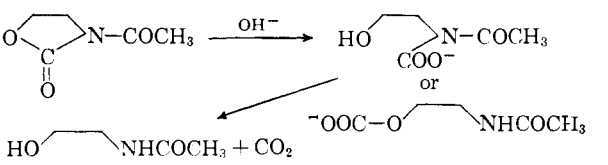
$$\text{Meq. compd. in reacn. mixt.} = \frac{K \times 0.1}{(A_{max} - A_{background}) \times M}$$

The frequencies used for the analyses are given in Table VI.

It was necessary to confirm that the other products of the hydrolysis reaction did not interfere at these wave lengths. Reaction mixtures for each compound were prepared as above. They were extracted with chloroform to remove lactam, the presence of the latter in the organic extracts being checked by infrared. The remaining water solutions were then found to be transparent in the infrared at the chosen wave length in all cases except for the pyrrolidone derivatives. This interference was not caused by unextracted pyrrolidone, since other characteristic bands of this lactam were absent. The analysis of the reaction mixtures containing pyrrolidone, therefore, was accomplished by adding known amounts of pyrrolidone to the reaction mixture, measuring the absorbance, and extrapolating back to no addend. The products from N-isobutyrylpyrrolidone interfered with the infrared analysis, and vapor phase chromatography was employed in this case.

From these analyses the observed over-all rate constant was split into the rate constants for attack at the acyl carbonyl and at the ring carbonyl. The results of these calculations are given in Table II.

One ambiguity should be noted in the case of the cyclic urethans and ureas. The reaction may proceed by two different courses which lead to the same product. For example,



The observed rate constants k_2 must be regarded as the sum of these processes.

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