

On the Isomerism of Hydroxyurea

X. Kinetics of the Isomerization

HELMER KOFOD

Royal Danish School of Pharmacy, Dept. of Organic Chemistry, Copenhagen, Denmark

The kinetics of the conversion of the lower melting isomeride in alkaline buffers, pH 9.2–12.3, have been examined, using a polarographic method of analysis.

At 25°C and pH 12 the reaction conformed to the empirical expression $Bt = \log(c_0/c) + A(c^{-1} - c_0^{-1})$. The constant A did not vary significantly with concentration in the range 1 to 8 mM but appeared to decrease with increasing pH, the overall reaction thus approximating to first-order kinetics in strongly alkaline solution.

At elevated temperatures and pH 12 the isomerization appears to be complicated by partial decomposition of the reactant into hydroxylamine and cyanate, in close analogy to the established chemical reversibility of the classical Wöhler synthesis of urea.

In the course of a general investigation on the polarographic behaviour of the lower melting isomeride (OU₇₂) it was previously observed (Ref. ¹, Fig. 1) that on remeasurement of alkaline aqueous solutions, stored at 25°C, the characteristic cathodic wave rapidly vanished. In slightly alkaline and neutral buffers the process was found to be much slower, and in acidic buffers no diminution of the wave was noticed within a period of 72 h, (Ref. ¹, Table 1).

It is fortunate that the pH-region, ca. 9–13, in which the isomerization proceeds at a convenient velocity also happens to be the most favourable one for polarographic analysis (Ref. ¹, Fig. 2). It was feasible, therefore, if desired to follow the advancement of the isomerization in the polarographic cell itself. The OU₇₂-wave is well developed in this pH-region, and the isomerization product, OU₁₄₀, does not produce any interfering wave. Previously published paper-chromatographic work of a qualitative nature ² suggested that in alkaline solution the conversion process might be sufficiently simple to justify a closer kinetic examination.

THE pH-DEPENDENCY OF THE ISOMERIZATION $\text{OU}_{72} \rightarrow \text{OU}_{140}$ AT 25°C

In the first series two experiments were carried out with 0.1 M potassium borate buffers at pH 10.5 and 12.3, respectively. The composition of the buffers and general technique are described p. 1077. The initial concentration of OU_{72} was 5.0 mM in both experiments.

5 ml of potassium borate buffer at pH 10.5 containing 0.1 % methylcellulose as a maximum suppressor was deaerated in the polarographic cell and the absence of dissolved oxygen was secured polarographically at high sensitivity. 1.90 mg of OU_{72} was weighed out and quickly dissolved in the cell contents (zero time). Polarographic recordings were run at time intervals. The results are listed in Table 1; t is the time in minutes from the dissolution of the solid until the maximum wave-height was attained during the recording of the polarogram. This point on the wave was reached 3 min after the recording had been started, the scanning speed being 1/3 V per min.

Table 1. Isomerization of OU_{72} at pH 10.5 and 25°C; initial concentration $c_0 = 5.0$ mM; capillary No. 1.

t	i	$10^3 \log (c_0/c)$	$10^4 k_1$
0	$(i_0) = 39.3$	0	
6	39.3	0	
10	39.3	0	
14	39.3	0	
18	39.3	0	
23	39.3	0	
33	38.7	6	4.2
63	38.0	14	5.1
123	36.7	29	5.4
251	33.5	69	6.3
303	32.5	82	6.3
440	29.5	124	6.5
513	27.0	163	7.3
590	26.0	179	7.0
657	24.7	201	7.0
1 307	17.7	346	6.1
1 547	14.1	445	6.0

In the next column i represents the diffusion current in μA , calculated from from the wave-height. The data are plotted in Fig 1, upper curve. The experimental points fit a straight line; although this suggests a zero-order reaction, it should be remembered that the degree of advancement in this experiment amounts to about 30 % only.

The reaction was accelerated in the next experiment by raising the pH to 12.3, other conditions remaining as above. The data are listed in Table 2, columns 1—2, and graphically represented in Fig 1, lower curve. The degree of advancement in this experiment is 98 %. The remaining data in Table 2 will be discussed under the heading "Order of reaction", p. 1073.

Table 2. Isomerization of OU_{72} at pH 12.3 and 25°C; capillary No. 1; initial concentration $c_0 = 5.0$ mM; $f(c) = \log(c_0/c) + 0.20(c^{-1} - c_0^{-1})$.

t	i	$10^3 \log(c_0/c)$	$10^3 k_1$	$10^3 f(c)$	$t_{\text{calc.}}$
0	40.0	0		0	0
5	36.7	37		41	0
8	35.3	54		59	5
13	33.3	80		88	12
18	32.0	97	12.4	107	17
23	30.7	115		127	22
28	29.3	135		150	27
33	28.0	155	10.8	172	33
43	26.0	187		268	42
53	24.0	222		249	52
63	22.0	260		293	63
73	20.5	290	9.2	328	71
83	19.0	323		367	82
93	17.3	364		417	94
103	16.3	390		448	102
113	15.0	426	8.7	493	114
128	13.3	478		558	129
148	11.7	534		631	148
163	10.3	589	8.4	704	166
183	9.3	633		766	182
198	8.5	673		821	195
213	7.6	721	7.9	892	213
233	6.8	769		964	231
253	6.1	817		1 041	250
273	5.5	862	7.3	1 113	268
293	4.9	912		1 198	290
318	4.4	959		1 282	310
343	3.6	1 036	7.1	1 441	350
363	3.3	1 083		1 528	372
393	3.1	1 111		1 586	387
428	2.5	1 204		1 804	441
468	2.3	1 240	6.1	1 896	464
520	1.4	1 456		2 560	630
1 169	0.8	1 699	3.4	3 651	901
1 423	0.7	1 757			

In another series of experiments, Tables 3–6, the initial concentration was fixed at $c_0 = 2.0$ mM, and measurements were carried out in phosphate buffers at pH 12.3 and 11.5, a carbonate buffer at 10.7 and a borate buffer at 9.2. A 20.0 mM stock-solution of OU_{72} in redistilled water was freshly prepared, and 5.4 ml of the appropriate buffer solution was measured into the thermostated polarographic cell and deaerated; 0.6 ml of the stock solution was added (zero time). Immediate mixing was secured by passing the nitrogen stream through the cell for another minute, and polarograms were recorded at suitable time-intervals. The experiment at pH 12.3 (Table 3) was carried out separately, whereas the solutions at pH 11.5, 10.7 and 9.2 (Tables 4–6) were measured intermittantly in one and the same experiment. The cells were stored, well stoppered, in the thermostat at 25.0°C and removed for polarographic recording, according to a minute rota. The experimental data

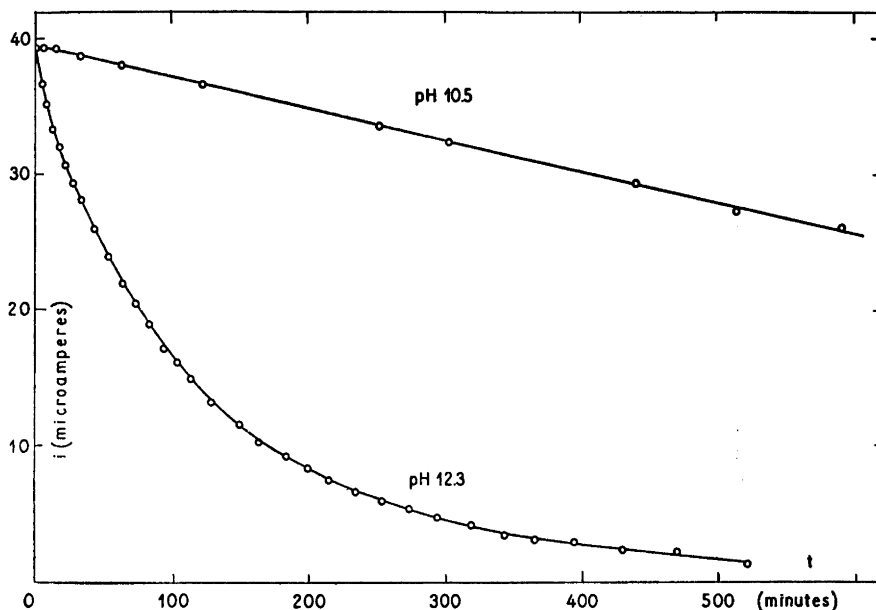


Fig. 1. Isomerization of OU_{72} at $25^{\circ}C$. Polarographic wave-height against time. Initial concentration $c_0 = 5.0$ mM. Data in Tables 1 and 2.

in Tables 3—6 are graphically represented in Fig 2. As above t represents the time in minutes from the mixing of the stock solution with the appropriate buffer until the maximum wave-height was attained during the recording of the individual polarogram.

CONCENTRATION DEPENDENCY OF THE ISOMERIZATION AT pH 12.0 AND $25^{\circ}C$

On the basis of the preceding experiments the potassium phosphate buffer at $pH \approx 12$ was selected for the investigation of concentration influences upon the rate of isomerization.

In planning the experiment in detail the following had to be taken into account: (1) In order to keep the autoisomerization of the unbuffered stock solution at a negligible level the experiment should be carried out within a single day; (2) Recording of the requisite part of the polarogram from -0.8 to 1.8 V vs. SCE required 3 min. Rinsing and wiping off the electrodes and changing from one cell to another took a further 2 min; (3) The concentrated solutions should be measured every 5 min at the outset and every 10 and 20 min at later stages. The dilute solutions should be measured every 20 min from the outset; (4) The zero time for the respective solutions should be arranged so as to avoid too frequent alterations in the set sensitivity of the polarographic instrument.

These requirements were met by the rota indicated in Tables 7a and 7b.

Table 3. Isomerization of OU_{72} at pH 12.3 and 25°C; capillary No. 2; initial concentration $c_0 = 2.0 \text{ mM}$; $f(c) = \log(c_0/c) + 0.20(c^{-1} - c_0^{-1})$.

t	i	$10^3 \log(c_0/c)$	$10^3 k_1$	$10^3 f(c)$
0	16.6	0		0
4	16.3	8		10
7	16.1	13	4.27	16
12	15.6	27		34
18	15.1	41	5.25	51
23	14.9	47		59
30	14.4	62	4.76	77
36	14.0	74		93
44	13.5	90		113
55	12.6	120	5.03	152
63	12.1	141		178
73	11.6	155		198
82	11.2	175		223
99	10.5	199	4.63	257
108	10.2	211		274
115	9.8	229		299
127	9.3	251		330
140	9.0	266	4.38	351
155	8.5	291		386
181	7.8	328		441
207	7.2	363		494
228	6.5	407		563
252	6.0	442		619
278	5.5	480	3.98	682
304	5.0	521		753
333	4.7	548	3.80	802

Table 4. Isomerization of OU_{72} at pH 11.5 and 25°C; capillary No. 2; initial concentration $c_0 = 2.0$; $f(c) = \log(c_0/c) + 0.20(c^{-1} - c_0^{-1})$.

t	i	$10^3 \log(c_0/c)$	$10^3 k_1$	$10^3 f(c)$
0	16.6	0		0
5	16.6	0		0
9	16.6	0		0
36	15.4	32	2.0	40
60	14.9	47	1.8	58
90	14.0	74	1.9	93
120	13.5	90	1.7	112
150	13.1	113	1.7	140
180	12.4	127	1.6	161
210	11.7	152	1.7	194
240	11.4	163	1.6	209
270	10.7	191	1.6	246
301	10.5	199	1.5	257
361	9.6	238	1.5	311
427	8.6	285	1.5	378
480	7.9	322	1.6	432
1 465	1.7	990	1.6	1 865

Table 5. Isomerization of OU_{72} at pH 10.7 and 25°C; $c_o = 2.0$ mM; capillary No. 2.

t	i	$10^3 \log (c_o/c)$
0	16.6	0
5	16.6	0
35	16.6	0
60	16.3	8
90	16.1	13
120	15.9	21
150	15.6	27
180	15.4	32
210	15.4	32
270	15.1	41
331	14.9	47
391	14.7	53
451	14.5	59
1 435	8.2	306

Table 6. Isomerization of OU_{72} at pH 9.2 and 25°C; $c_o = 2.0$ mM; capillary No. 2.

t	i	$10^3 \log (c_o/c)$	$10^3 k_1$
0	16.6	0	
5	16.6	0	
30	16.6	0	
60	16.3	8	3.1
91	16.1	13	3.3
120	16.1	13	2.5
150	15.9	19	2.9
210	15.4	32	3.5
271	15.4	32	2.7
331	15.4	32	2.2
1 317	11.0	178	3.1

An aqueous stock solution containing 10.0 mmoles/l of OU_{72} was freshly prepared, deaerated and stored in a well-stoppered flask. Solution No. 1 was prepared by mixing stock solution and buffer in appropriate proportions to give an initial concentration of 8.0 mM. The zero time was 10 o'clock (Table 7a) and polarographic recordings were run according to Table 7b. When this reaction had slowed down solution No. 2 was started *etc.* The

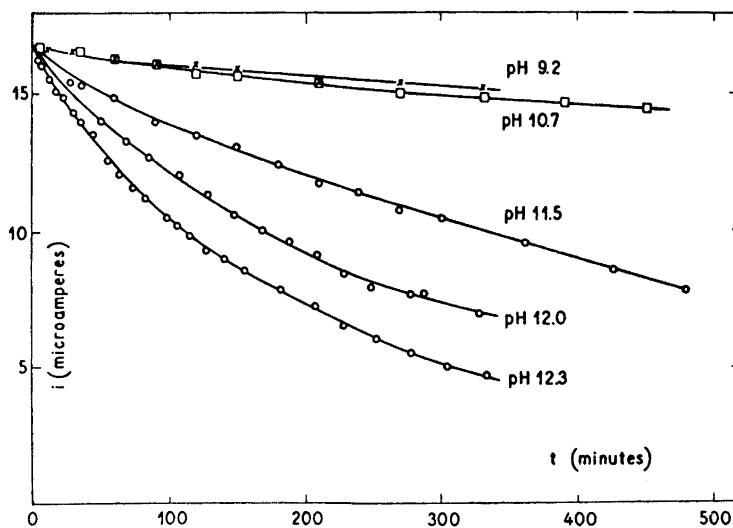


Fig. 2. Isomerization of OU_{72} at 25°C; pH dependency. Polarographic wave-height against time. Initial concentration $c_o = 2.0$ mM. Data in Tables 3-6 and 11.

Table 7 a.

Solu- tion	c_0	Zero time
1	8.0	10 ^h 0 min
2	6.0	11 ^h 5 min
3	4.0	12 ^h 5 min
4	2.0	13 ^h 0 min
5	1.0	15 ^h 15 min

Table 7 b. Time for commencement of polarographic recordings in Tables 8–12.

h min.	10	11	12	13	14	15	16	17	18	19	20
	2				4	4	4	4	4		4
7	1	2	3	3	3	3	3	3		3	
12	1	2	2	2	2	2	1	2	1		5
17	1	1	1	1	1	5	5	5	5	5	
22	1	2		4	4	4	4	4	4		
27	1		3	3	3	3	3		3		
32		2	2	2	2	1	2	1	2	4	
39	1	1	1	1	1	5	5	5			
42		2		4	4	4	4	4			
47	1		3	3	3	3	3	3		3	
52		2	2	2	2	2	1	2			
57	1	1	1	1	1	5	5	5	5	5	

solutions were prepared in separate polarographic cells. They were stored in a thermostat at 25.0°C and removed periodically for recording.

The experimental data are collected in Tables 8–12; t represents the time in minutes from zero time, defined as above, until the maximum wave-height was attained during the recording.

Table 8. Isomerization of OU_{72} at pH 12.0 and 25°C; $c_0 = 8.0$ mM; capillary No. 2; $f(c) = \log (c_0/c) + 0.8 (c^{-1} - c_0^{-1})$.

t	i	$10^3 \log (c_0/c)$	$10^3 f(c)$
0	66.4	0	0
11	63.0	2	3
16	65.0	9	11
23	62.0	30	37
30	60.0	44	55
35	59.0	51	63
43	56.0	74	92
54	53.0	98	123
63	51.0	114	144
84	48.0	141	179
103	44.0	179	229
123	40.0	220	285
143	38.0	242	316
163	35.0	278	367
183	32.0	318	427
203	30.5	338	455
223	28.0	375	511
243	26.5	399	549
264	24.5	433	603
283	23.0	460	648
303	21.5	490	697
338	19.5	532	771
378	17.3	584	866
418	15.4	636	965
458	14.0	676	1 047
498	12.7	718	1 137

Table 9. Isomerization of OU₇₂ at pH 12.0 and 25°C; c₀ = 6.0 mM; capillary No. 2; f(c) as in Table 8.

<i>t</i>	<i>i</i>	10 ³ log (c ₀ /c)	10 ³ f(c)
0	49.8	0	0
8	49.0	7	9
14	48.0	16	21
23	47.0	25	34
33	45.0	44	58
43	42.0	74	100
53	40.0	95	127
73	37.3	129	173
93	34.0	165	226
113	31.3	201	279
133	28.5	242	341
153	26.5	274	390
173	24.5	308	444
193	22.7	341	499
213	21.0	375	553
233	19.7	403	605
253	18.0	442	676
293	15.9	496	778
333	14.2	545	884
373	12.6	597	988
413	11.3	644	1 094
453	10.3	684	1 192

Table 10. Isomerization of OU₇₂ at pH 12.0 and 25°C; c₀ = 4.0 mM; capillary No. 2; f(c) as in Table 8.

<i>t</i>	<i>i</i>	10 ³ log(c ₀ /c)	f(c)
0	33.2	0	0
8	32.0	16	24
28	30.0	44	65
48	27.3	85	128
68	24.5	132	203
88	23.1	157	246
108	21.5	189	297
128	19.3	235	378
148	18.3	258	420
168	17.3	283	466
188	16.0	317	531
208	14.7	354	604
228	13.5	391	681
248	12.8	414	731
268	12.1	438	784
288	11.4	464	844
308	10.5	500	930
348	9.5	543	1 039
388	8.7	581	1 141
428	7.8	629	1 276
468	7.3	658	1 363

Table 11. Isomerization of OU₇₂ at pH 12.0 and 25°C; c₀ = 2.0 mM; capillary No. 2.

<i>t</i>	<i>i</i>	10 ³ log(c ₀ /c)
0	16.6	0
8	16.5	2
28	15.5	30
49	14.0	74
68	13.3	96
85	12.7	116
108	12.0	141
128	11.3	167
148	10.5	199
168	10.0	220
188	9.6	238
208	9.1	261
228	8.4	296
248	7.9	321
278	7.7	333
288	7.7	333
328	7.0	375
369	6.8	387
398	6.7	394
438	6.5	407

Table 12. Isomerization of OU_{72} at pH 12.0 and 25°C; $c_0 = 1.0$ mM; capillary No. 2.

t	i	$10^3 \log(c_0/c)$
0	8.3	0
8	7.3	56
28	7.2	62
48	7.0	74
68	6.3	121
89	6.1	134
108	5.8	156
128	5.4	187
148	5.5	179
168	5.3	195
188	5.3	195
230	5.0	220
248	5.0	220
288	5.0	220
303	4.8	238

Table 13 (cf. Fig. 3).

Stoichiometric c_0 , mM	i_0 *, μA	Extrapolated (timelag assumed) i_0 , μA	Inflection point min.
8.0	66.4 ± 0.5	67.0 ± 1.0	18 ± 3
6.0	49.8	50.0 ± 1.0	25 ± 10
4.0	33.2	32.5 ± 1.0	30 ± 15
2.0	16.6	16.5 ± 1.0	35 ± 15
1.0	8.3	8.0 ± 1.0	40 ± 15

* calculated by means of the relation $i = 8.3 c$.

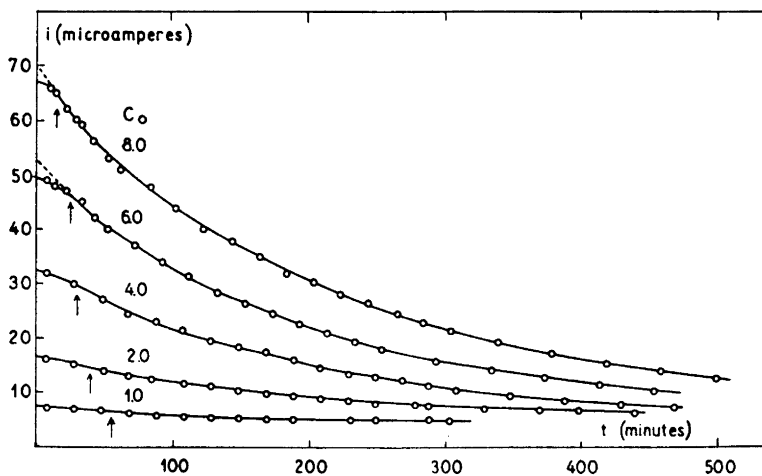


Fig. 3. Isomerization of OU_{72} at 25°C and pH 12.0. Influence of initial concentration c_0 . Polarographic wave-height against time. Data in Tables 8–12.

The results are graphically represented in Fig. 3. The polarographic wave height i in μA has been plotted against time and the experimental points were visually fitted with the best curve. The initial values of i ($t = 0$) were calculated from the stoichiometric concentration c_0 of OU_{72} by means of the relation $i = 8.3 c$ (Table 13)

On the graphs, Fig. 3, there appears to be a time-lag at the outset of the reaction. Although the irregularities are close to the experimental error, there is a definite trend in all the graphs, and furthermore the time-lag has to be assumed in order to get a reasonable accordance, *cf.* Table 13, between the stoichiometric value for the initial wave-height i_0 and the extrapolated one. Extrapolation from the main part of the graph ($t > 50$ min) is seen to give too high initial values.

The pH of the solutions were checked at the end of the experiment. They all had pH 12.0 ± 0.1 .

ISOMERIZATION AT 35°C AND pH 12

In a provisional experiment the isomerization was studied in a phosphate buffer at pH 12 and at 35°C, the initial concentration was 6 mmoles/l. The reaction was quenched by reducing the pH to approximately 7; this was done by diluting withdrawn samples in the proportion 1:10 with the appropriate buffer; polarographic recordings of the dilutions were run immediately. The reaction was, however, found to be inconveniently rapid under these conditions and in a subsequent experiment it was slowed down by reducing the pH to 9.2, the temperature being maintained at 35°C.

CONVERSION PROCESSES AT 35°C AND pH 9.2

The initial concentration was 5.0 mmoles/l and the reaction was quenched in withdrawn samples simply by rapidly reducing the temperature to 25°C. Immediately upon temperature equilibration in the polarographic cell, recordings were run directly on the undiluted samples at pH 9.2. The current-voltage curves are reproduced in Fig. 4 Nos. 2–10. They display a characteristic

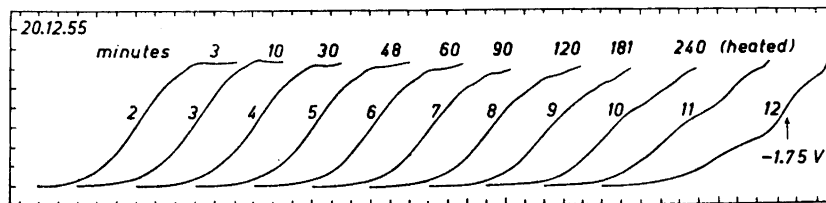


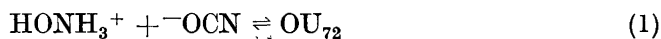
Fig. 4. Conversion of OU_{72} at 35°C and pH 9.2. Cathodic polarographic waves recorded at 25°C. Initial concentration $c_0 = 5.0$ mM. All waves begin at -0.8 V versus the saturated calomel electrode (SCE). One unit on the abscissa represents 0.1 V. One unit on the ordinate represents $6.66 \mu\text{A}$. Drop-time of mercury electrode 3.6 sec; rate of mercury outflow 2.46 mg sec^{-1} .

feature, which was not noticed at 25°C, namely the appearance of a new wave with a half-wave potential of approximately -1.75 V. In order to corroborate this observation a withdrawn sample from the reaction vessel was briefly heated to 80°C, cooled to 25° and polarographed (No. 11). The cell contents were heated once more to 80°C for 2 min and now produced curve No. 12, in which the new wave is clearly distinguishable.

A blank test with the supporting buffer alone proved that the new wave did not originate from the buffer or the vessel upon heating. Neither was it due to the isomerization product OU_{140} , since this has been shown to be polarographically inactive in the voltage region covered by these experiments.

A solution of 5 mg of OU_{140} in 5 ml borate buffer pH 9.2 was heated to 80°C for a short time and subsequently polarographed at 25°C. The current-voltage curve was identical with that of the buffer itself, even at a sensitivity increased by a factor 10. The isomeric hydroxyurea OU_{140} does not, therefore, appear to produce the wave at -1.75 V, observed in the experiment with OU_{72} under similar conditions.

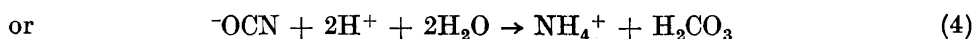
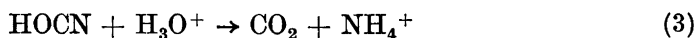
It appears reasonable to regard the wave as being due to hydroxylamine. The estimated half-wave potential -1.75 vs. S.C.E. is in accordance with the value previously determined for hydroxylamine (Ref.¹ p. 463, Fig. 6), and the formation of hydroxylamine in alkaline solution at elevated temperatures by reversion of the formation process



has a close analogy in the well-established reversibility — in the chemical sense — of the urea formation from ammonium cyanate



Walker and Hambley³ in 1895 first called attention to the reversibility of Wöhler's classical synthesis, and since then several authors have studied the kinetics of the reaction⁴. Although they all agree that ammonium cyanate is an intermediate in the decomposition, the numerical values of the rate constants differ and so do the proposed mechanisms. Lately the decomposition of urea in aqueous solution has been subjected to a careful investigation by Shaw and Bordeaux⁴. The reaction was studied at urea concentrations ranging from 6 to 1 200 mmoles/l at six different temperatures in the presence and absence of acid. The reaction is reported to be first-order with respect to urea and — contrary to the findings of other authors — uncatalyzed by acid. Within the experimental uncertainties the rate constants were the same in water and in acid, though with a slight trend towards higher rate constants in acid. This was explained by assuming that in water alone recombination of the ions to form urea occurs to a small degree. In acid this reaction is prohibited, because the cyanate ion formed by the decomposition (the reverse of reaction 2) is rapidly and quantitatively converted into ammonium ion^{4,5}.



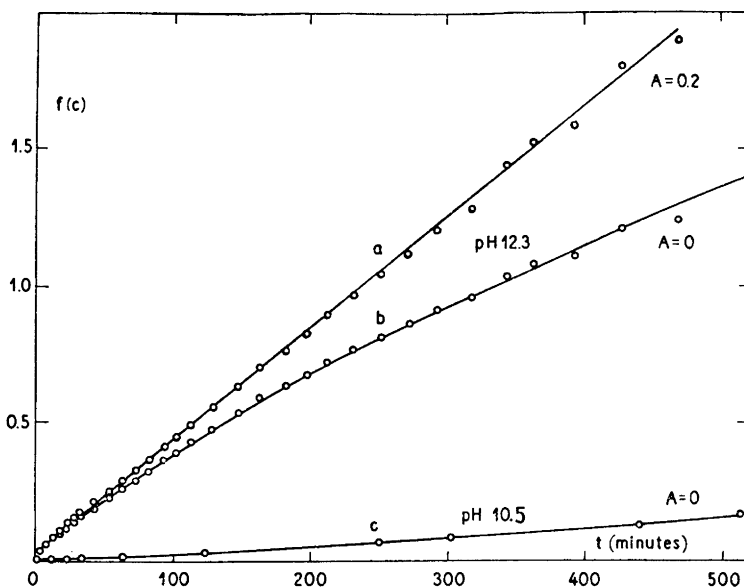


Fig. 5. Plot of the empirical function $f(c) = \log_{10} (c_0/c) + A(c^{-1} - c_0^{-1})$ against time; $c_0 = 5.0$ mM. Data in Tables 1 and 2.

Certain anomalies at high acid concentrations were explained as a result of the equilibrium $U + H^+ \rightleftharpoons UH^+$ (U standing for urea) assuming that the uronium ion UH^+ cannot be directly decomposed into ammonium cyanate. This has previously been postulated by several authors. The stability of OU_{72} in acid solution at room temperature⁶ (Ref.¹, Table 1), may be understood on similar grounds; this substance has even more pronounced basic properties than urea (Ref. ⁶, p. 498). OU_{140} on the other hand is a weak acid. The existence of a stabilized anion in alkaline solution may account for the fact that this substance does not decompose readily into hydroxylamine as shown above by polarographic tests.

ORDER OF REACTION

Since the isomerization at higher temperatures was found to be complicated by competing decomposition reactions, the discussion of the order of reaction will be based entirely on the data obtained at 25°C. The data on Table 2 obtained at pH 12.3 will first be considered on the basic assumption that they correspond to a simple isomerization mechanism, either a single reaction or a set of consecutive reactions.

The data were tested in the integrated first-order equation

$$k_1 t = 2.303 \log_{10} (c_0/c) \quad (5)$$

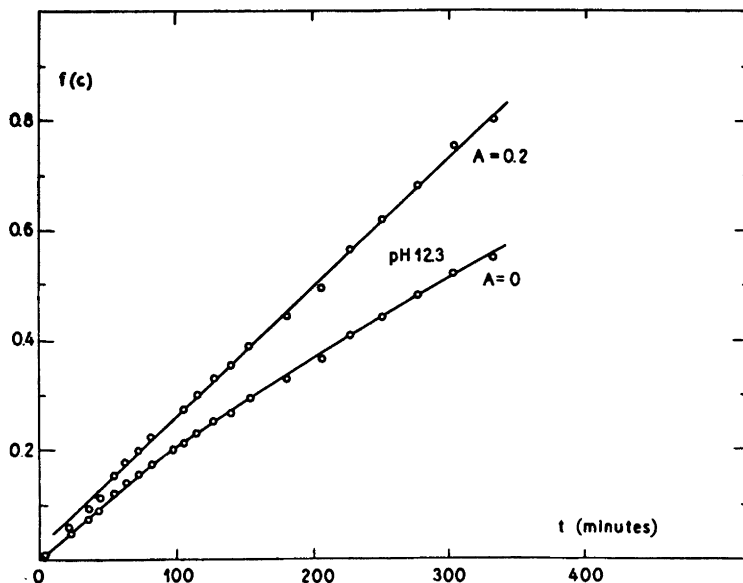


Fig. 6. Plot of the empirical function $f(c) = \log_{10} (c_0/c) + A(c^{-1} - c_0^{-1})$ against time $c_0 = 2.0$ mM. Data in Table 3.

c_0 being the initial concentration of OU_{72} and c the concentration at any time t . Since a linear relationship between concentration and polarographic wave-height i has been experimentally demonstrated, c_0/c may be replaced by i_0/i

$$k_1 t = 2.303 \log_{10} (i_0/i) \quad (6)$$

Calculated representative values for the first-order rate "constant" k_1 are given in Table 2, col. 4. The systematic drift of the "constant" indicates the invalidity of the assumption of first-order or pseudo-first-order kinetics. The same is obvious from the decided curvature of the graph Fig. 5 b, which in fact is a plot of $\log (c_0/c)$ versus t and hence should be linear. Salt effects have been neglected, but they are not apt to alter the order of reaction under the present conditions. Though the same reaction mixture was polarographed repeatedly, the consumption of OU_{72} due to the electrode process cannot be made responsible for the deviation. On the first hand it is of a negligible magnitude, and on the other hand it would give rise to an error in the opposite direction.

The data were then tested in the second-order equation

$$k_2 t = c^{-1} - c_0^{-1}$$

or

$$k'_2 t = i^{-1} - i_0^{-1} \quad (7)$$

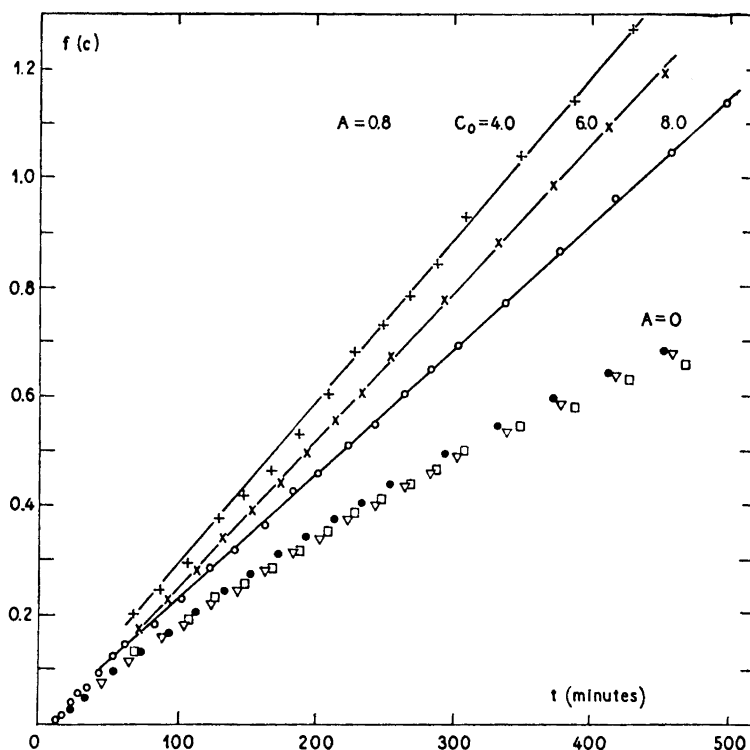


Fig. 7. Plot of the empirical function $f(c) = \log_{10}(c_0/c) + A(c^{-1} - c_0^{-1})$ against time. Data in Tables 8–10.

Non-linearity of the plot of i^{-1} versus t indicated that the reaction does not conform to second-order kinetics with respect to OU_{72} .

When general chemical observations are scarce, or present a complicated picture, it is customary to attempt by the method of trial and error to construct a combined function fitting the experimental data with reasonable accuracy. The procedure of Christiansen ⁷ for a linear sequence of reactions was adopted.

In the equation

$$t = B_1 \cdot I_1 + B_2 \cdot I_2 + \dots \quad (8)$$

t stands for time in minutes, $B_1, B_2 \dots$ are constants and $I_1, I_2 \dots$ are the common integrated kinetic expressions $c, \log(c_0/c), (c^{-1} - c_0^{-1}), (c^{-2} - c_0^{-2})$ etc. As above c_0 is the initial concentration and c the concentration remaining at any time t .

By selecting first- and second-order expressions, respectively, for I_1 and I_2 the modified function (9) was obtained.

$$Bt = \underbrace{\log_{10}(c_0/c)}_{f(c)} + \underbrace{A(c^{-1} - c_0^{-1})}_{f(c)} \quad (9)$$

By the method of hit and miss a value of the constant A was found, which upon insertion of the experimental sets of data c, t (Table 2) rendered the right-hand side of (9) a linear function of t (Fig. 5a). The value $A = 0.2$ is seen to give a satisfactory linearity, except for a short interval at the outset of the reaction (*cf.* p. 1073). The slope of the line is $B = 0.004$. Towards the end of the reaction the scattering is somewhat large, owing to experimental errors, but there is no systematic deviation from linearity up to 95 % advancement. The line does not pass exactly through the origin, but there is a small positive intercept on the ordinate axis. It is uncertain whether this is kinetically significant, but the empirical expression fitting the data in Table 2 is

$$0.004 t + 0.004 = \log_{10} (c_0/c) + 0.20(c^{-1} - c_0^{-1}) \quad (10)$$

For the sake of control values of t have been calculated from eqn. 10. They are included in Table 2, col. 6, and show a fair agreement with the experimental values.

The data in Table 3 were similarly tested in the empirical eqn. 9. In this experiment the pH was unaltered and equal to 12.3 within the accuracy of measurement, ± 0.1 , but the initial concentration of OU_{72} was $c_0 = 0.2$ mmoles/l. Fig. 6 ($A = 0$) shows the plot of $\log c_0/c$ versus t . It is decidedly curved, again indicating the invalidity of first-order kinetics. The upper graph represents the mixed function $f(c)$. The selected value of A , which rendered the plot linear, is the same (0.2) as previously found, but it should be pointed out that a reasonable linearity may be achieved for values of A between the limits 0.15 and 0.25 so that the accordance may be incidental rather than significant.

The crucial test of the validity of the empirical expression (9) is the independency of the constants A and B of concentration. The data in Tables 8–12 (*cf.* Fig. 3) were intended for this test. This series of experiments is not directly comparable with the previous ones, since the pH was somewhat lower (12.0). It appears from Fig. 7 that for the three highest concentrations a linear plot of $f(c)$ versus t is obtained when 0.8 is selected for the constant A . For the lower concentrations the experimental error gives rise to a considerable scattering of the calculated values of $f(c)$ and it is not possible to select a reasonably well-defined value of A to give linearity. There is no direct indication, however, that A varies with concentration, but this actually needs confirmation by experiments carried out at still higher concentrations. For such measurements, however, the polarographic method is unsuitable.

Table 14. Values of constants A and B (eqn. 9) at 25°C.

pH	12.3 b	12.3 p	12.0 p	12.0 p	12.0 p
c_0	5.0	2.0	8.0	6.0	4.0
A	0.2 ± 0.1	0.20 ± 0.05	0.80 ± 0.05	0.8 ± 0.1	0.8 ± 0.2
$10^3 B$	4.0 ± 0.5	2.3 ± 0.2	2.3 ± 0.1	2.7 ± 0.2	2.9 ± 0.5
Table	2	3	8	9	10
Fig.	5	6	7	7	7

* b borate buffer p phosphate buffer

The selected values of A and the graphically determined slopes B are summarized in Table 14, with the estimated errors.

The value of A seems to decrease rapidly with increasing pH. The overall process, therefore, seems to approximate to simple first-order kinetics in strongly alkaline solution, probably because a rapid, base-catalyzed, pseudo-first-order isomerization is predominating. In weakly alkaline or neutral solution the overall process seems to proceed by a more complicated sequence of reactions or alternatively by a mechanism of concurrent reactions. The possibility of decomposition into hydroxylamine and cyanate obviously should be taken into account, *cf.* p. 1072.

A discussion of reaction mechanisms in terms of the actual molecular structures will be presented elsewhere in a larger context.

MATERIALS AND GENERAL TECHNIQUE

The preparation and characterisation of the isomeric oxyureas have been reported in a previous publication⁸. Freshly prepared samples were used.

All chemicals used for preparing the supporting buffer-solutions were analytical grade products. The solvent was water, carefully redistilled in Pyrex apparatus.

The compositions of the buffer stock solutions are indicated in Table 15.

Table 15. Composition of buffer stock solutions.

- A. 1 M boric acid, 1 M potassium dihydrogen borate
- B. 1 M potassium monohydrogen phosphate
- C. 1 M potassium hydrogen carbonate
- D. 1 M potassium hydroxide

The set of stock solutions used in the various experiments are given in Table 16. Unless otherwise stated appropriate volumes were mixed and diluted to the tenfold volume with water containing 0.02 % methylcellulose as a maximum suppressor.

The instrument for measurement of the pH as well as the polarographic equipment and technique have been described in a previous paper (Ref¹, p. 468–469).

Table 16.

Experiment		pH	Stock solutions		Buffer type
Table	Fig.		(c ₀ . Table 15)		
1	1	10.5	A	D	borate
2	1	12.3	A	D	borate
3	2	12.3	B	D	phosphate
4	2	11.5	B	D	phosphate
5	2	10.7	C	D	carbonate
6	2	9.2	A		borate
8–12	3	12.0	B	D	phosphate

Two different capillaries were used for the dropping mercury electrode in the present experiments. The characteristic data for No. 1, employed in the experiments, Tables 1 and 2, were as follows; height of mercury column 45 cm, drop time 3.3 sec, rate of mercury outflow into water 2.7 mg sec⁻¹. The experimental relationship between wave-height i

(diffusion current in μA) and concentration c of OU_{73} was $i/c = 8.0$; (cf. Ref.¹, Fig. 4.) Capillary No. 2, employed for the rest of the experiments (Tables 3–6 and 8–12) had the following characteristics; heights of mercury column 23 cm, drop time 3.0 sec, rate of mercury outflow into water 3.0 mg sec^{-1} . The relation between wave-height and concentration for this capillary was $i/c = 8.3$. The conversion factor cannot be determined directly at pH 12 and 25°C with any great accuracy, owing to the rapid isomerization of the substance. It has been established for the employed capillary by measurements of a series of concentrations at pH 9.2, and it is assumed that the same conversion constant is valid at pH 12.2. The assumption is justified by previous experiments (Ref.¹, Fig. 2) showing that the wave-height for a given concentration does not vary significantly with pH in the region 6.3–12.3.

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