672. *Nitramines and Nitramides. Part VI.* Some* N-*Nitrations in Solvents Other than Sulphuric Acid.*

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In contrast with the behaviour in sulphuric acid, the nitrations of urethane, *N*-methylurethane, and urea are not reversible in acetic anhydride–acetic acid. Urethane is not nitrated in acetic acid as solvent. The nitrations of urethane and of guanidine are reversible in 60% perchloric acid, or in selenic acid.

When urethane, *N*-methylurethane, or urea was allowed to react with one molecular proportion of nitric acid in, essentially, acetic anhydride ($Ac_2O : AcOH = 96 : 4$, w/w) the concentration of free nitric acid fell, but did not tend towards an equilibrium value. No nitric acid was set free when the corresponding nitramides were dissolved in the same solvent. The indicated yields in the nitration process were good (60—80% after one hr. at 25°). Urethane and urea were nitrated at similar speeds, but *N*-methylurethane was nitrated more rapidly. More precise conclusions seem unwise: we measured the concentration of nitric acid, and this may be reduced by reactions other than the nitration of the amides. The reaction between nitric acid and acetic anhydride is the most obvious of these, though probably of little significance in the time available. It was qualitatively possible to isolate the nitramides, and we believe that the yields quoted in this, and the next, paragraph are accurate to within 5%. A fuller discussion is postponed to the Experimental section.

The nitration of urethane has also been investigated in other acetic anhydride–acetic acid mixtures, and in acetic acid alone. In mixtures containing acetic anhydride ($Ac_2O : AcOH = 50 : 50$, w/w; and $Ac_2O : AcOH = 5 : 95$, w/w) nitration took place, though more slowly: the indicated yields were 80 and 40%, respectively, after 20 hours at 25°. In acetic acid ($AcOH : H_2O = 99{\cdot}5 : 0{\cdot}5$, w/w) no nitration could be detected. It appears that some acetic anhydride (or, possibly, the absence of water) is necessary; and

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* Part V, preceding paper.

the non-reversibility of the reaction indicates clearly why most workers have empirically preferred acetic anhydride to sulphuric acid as a solvent medium for *N*-nitration.

The nitrations of urethane and guanidine have been found to be reversible in 60% perchloric acid; the processes were slower than in concentrated sulphuric acid, but, by working at 70°, urethane and guanidine were brought to equilibrium with the corresponding *N*-nitro-compounds in, respectively, 20 minutes and 10 hours. The yields indicated were *ca.* 53% of nitrourethane and *ca.* 21% of nitroguanidine. Irreversible decomposition could be detected after prolonged heating at 70°, but did not appear to be significant in periods of up to an hour for nitrourethane, or 15 hours for nitroguanidine; the same equilibrium values were obtained by the use of nitrourethane and nitroguanidine as initial materials.

The behaviour of selenic acid as a solvent has been investigated briefly. Addition of nitrourethane or nitroguanidine to acetanilide in selenic acid (91·0%, w/w) gave *p*-nitroacetanilide in yields comparable with those previously obtained (Part III, *J.*, 1952, 1886) by the use of sulphuric acid.

It was found impossible to make a 0·2M-solution of guanidine nitrate in acetic anhydride–acetic acid (96 : 4, w/w), and guanidine nitrate was precipitated when nitric acid was added at 25° to a solution made up from guanidine carbonate and the solvent. The nitration of guanidine in acetic anhydride could not, therefore, be compared quantitatively with that of the urethanes or of urea.

EXPERIMENTAL

The solutions were made up, and analysed for free nitric acid in the presence of *N*-nitro-compounds, in the manner previously described (Part V, *loc. cit.*; Simkins and Williams, *J.*, 1952, 3086). When required, nitric acid (70%, w/w) was added immediately before the introduction of the amide, and the solvent compositions reported take into account the water thus added. Blank trials, and standardisation by means of potassium nitrate, showed that neither acetic nor perchloric acid affected the determination of nitric acid.

TABLE 1. *Fall in nitric acid, initially* 0·2M *in acetic anhydride–acetic acid media. caused by urethane,* N-*methylurethane, or urea*

Initial amide concn., 0·2M. Temp. 25° ± 0·2°.‡ Times are in minutes.

Expt. 1. Urethane and nitric acid in Ac_2O : AcOH = 96 : 4, w/w.									
t	10	22	37	57	90	126	169	270	375
[HNO_3] ...	0·1463	0·1177	0·0977	0·0843	0·0710	0·0629	0·0549	0·0472	0·0417
Expt. 2. *N*-Methylurethane and nitric acid in Ac_2O : AcOH = 96 : 4, w/w.									
t	11	22	39	60	93	150	250	357	
[HNO_3] ...	0·0719	0·0563	0·0464	0·0394	0·0330	0·0273	0·0224	0·0196	
Expt. 3. Urea and nitric acid in Ac_2O : AcOH = 96 : 4, w/w.									
t	10	22	39	61	91	150	256	383	
[HNO_3] ...	0·1730	0·1377	0·1088	0·0852	0·0684 †	0·0517 †	0·0396 †	0·0331 †	
Expt. 4. Urethane and nitric acid in Ac_2O : AcOH = 50 : 50, w/w.									
t	10	28	59	120	270	450	702	1338	
[HNO_3] ...	0·1750	0·1484	0·1237	0·0990	0·0739	0·0608	0·0503	0·0390	
Expts. 5, 6. Urethane and nitric acid in Ac_2O : AcOH = 5 : 95, w/w.									
t (Expt. 5)	11	26	65	150	267	395	1123		
[HNO_3] ...	0·1973	0·1955	0·1896	0·1800	0·1685	0·1584	0·1247		
t (Expt. 6)	731	1470	2171	2959	3765	5435			
[HNO_3] ...	0·1396	0·1154	0·1020 †	0·0914 †	0·0839 †	0·0727 †			

† These values are probably lower than would be the case if HNO_3 were removed solely by nitration of the amide. Values so marked correspond to the loss of 5% (or more) of HNO_3 from solutions of HNO_3 (0·2M) and the nitramide (0·2M) in the same solvent: it has been assumed that the solvent of Expt. 4 would behave like that of Expt. 5.

‡ Room temperature (*ca.* 20°, uncontrolled) during initial mixing (3 min.).

Nitration of the Urethanes in Acetic Anhydride–Acetic Acid Media.—The decreases in nitric acid concentration are given in Table 1; they do not necessarily indicate the extent of nitration. First, nitric acid may be removed by reaction with acetic anhydride. A blank experiment, in the absence of urethane, showed that the concentration of nitric acid in acetic anhydride ($Ac_2O : AcOH = 96 : 4$, w/w) fell only from 0·2000 to 0·1950M in 6 hr. at 25°. In the actual experiments the concentration of nitric acid was, for most of the time. less than 0·1M, and therefore the loss from this source was presumably smaller than that observed in the blank. We have assumed that the reaction would not be significant in the media containing 50 or 95% of acetic acid, and consider that losses from this source do not lead to a significant over-estimation of the degree of nitration.

Secondly, the residual nitric acid may react with the nitramide (or decomposition products thereof). We were unable, through bluntness of the end-point, to determine the total nitric acid (free and available from $>N{\cdot}NO_2$) by electrometric titration of samples dissolved in an excess of concentrated sulphuric acid. Instead, solutions were made up containing the nitramide (0·2M) and nitric acid (0·2M) : the losses from these solutions were presumably greater than those in the main experiments, where both solutes were present in lower concentration. In acetic anhydride ($Ac_2O : AcOH = 95 : 4$, w/w) the concentration of nitric acid in the presence of nitrourethane fell from 0·2000 to 0·1943M in 6 hr. at 25°, a loss similar to that observed in the absence of nitrourethane. We have assumed that the loss would be no greater in the presence of *N*-methylnitrourethane, which is known to be more stable to acid reagents.

On the other hand, a loss (0·2000 to 0·1989, 0·1937, 0·1852, 0·1773, and 0·1699M in, respectively, 0·8, 17·1, 42·4, 68·2, and 90·0 hr. at 25°) was found when nitric acid was kept, in the presence of nitrourethane, in acetic acid containing a little anhydride ($Ac_2O : AcOH = 5 : 95$, w/w). We do not suggest that these losses were due to the change from the anhydride to the acid : in the predominantly acid medium the time involved was much greater. Nitration, however, was slow in the acid ($Ac_2O : AcOH = 5 : 95$, w/w) medium, and it seems likely that after, say, 25 hr. the (observed) fall in nitric acid may be significantly greater than that due to nitration alone.

Nitration of Urea in Acetic Anhydride–Acetic Acid (96 : 4, w/w).—The fall in nitric acid concentration is given in Table 1; it is subject to the same limitations as that discussed above. The loss of nitric acid from a solution (initially 0·2M in nitric acid and in nitrourea) in acetic anhydride ($Ac_2O : AcOH = 96 : 4$, w/w) was comparatively rapid : the residual free nitric acid was 0·1947, 0·1868, 0·1683, 0·1625, 0·1479, and 0·1428M after, respectively, 21, 76, 214, 270, 344, and 378 min. at 25°. It thus appears that in the case of urea in acetic anhydride ($Ac_2O : AcOH = 96 : 4$, w/w), the reduction in nitric acid may be significantly greater (after the first hour) than that due to nitration alone. It can be seen, from Table 1, that the observed fall in nitric acid was initially greater in the presence of urethane, but finally greater in the presence of urea. We consider this to be due simply to the more rapid removal of nitric acid by nitrourea (or its decomposition products).

Irreversibility of Nitration in Acetic Anhydride.—0·2M-Solutions of nitrourethane, *N*-methylnitrourethane, or nitrourea in acetic anhydride ($Ac_2O : AcOH = 96 : 4$, w/w) were kept at 25°, and yielded no free nitric acid (within experimental error) in periods of up to 6 hr. (Maximum $[HNO_3]$ found, 0·0006M.)

Absence of Nitration in Acetic Acid Alone.—A solution of urethane (0·2M) and nitric acid (0·2M) in acetic acid ($AcOH : H_2O = 99{\cdot}5 : 0{\cdot}5$, w/w) was kept at 25°, and showed no fall in free nitric acid (within experimental error) in periods of up to 18 hr. (Minimum $[HNO_3]$ found, 0·1995M.)

Qualitative Isolation of the Nitramides.—(*a*) Urea nitrate (10 g.) was added to acetic anhydride–acetic acid (30 : 5 ml.) at 60°. After 35 min. at 60° the solution was cooled in ice, and crude nitrourea (2·5 g.; m. p. 143°, decomp.) collected. Two crystallisations from alcohol yielded pure material, identified by mixed m. p. and formation of the *S*-benzylthiuronium salt. (*b*) Urethane (13·5 g.) was added portionwise, below 25°, to a mixture of acetic anhydride (30 ml.) and nitric acid (11 ml. of 98%). After 1 hr. at 20—25°, the solution was poured into water, and extracted with ether, and the extract washed once with water. Part of the washed extract was dried and evaporated (finally *in vacuo* over KOH) to yield nitrourethane, m. p. 59—63°; the remainder was treated with gaseous ammonia to precipitate salts, from which pure ammonium nitrourethane could be obtained by one crystallisation from alcohol. (*c*) The preparation of *N*-methylnitrourethane in good yield in an acetic anhydride medium has been reported by Curry and Mason (*J. Amer. Chem. Soc.*, 1951, **73**, 5043).

Experiments in Perchloric Acid.—The results are given in Table 2. Equilibrium values were obtained, as explained in Part V (*loc. cit.*), by extrapolation back to zero time : since little irreversible decomposition was apparent in the course of the experiments, these values do not differ greatly from the final (observed) concentration of nitric acid. The sampling pipette was calibrated (by weight delivered) in terms of molarity at 25°, and the molarity of nitric acid reported is thus that which would have occurred in the solution after sudden cooling, without chemical change, to 25°. Owing to thermal expansion, the true molarities at 70° must have been somewhat smaller.

TABLE 2. *Reversible nitrations of urethane and guanidine in* 60% *perchloric acid at at* 70° ± 0·2°.

Molarity of HNO_3 in terms of solutions at 25°; times are in minutes.

Expt. 7. Urethane and nitric acid (both 0·2M at 25°) in perchloric acid (60·1%, w/w).
Equil. val. : $[HNO_3]$, 0·094M.

t	8	16	27	41	55	75
$[HNO_3]$	0·1189	0·0953	0·0930	0·0928	0·0920	0·0907

Expt. 8. Nitrourethane (0·2M at 25°) in perchloric acid (60·8%, w/w).
Equil. val. : $[HNO_3]$, 0·095M.

t	6	16	26	36	60	77
$[HNO_3]$	0·0558	0·0926	0·0941	0·0940	0·0919	0·0894

Expts. 9, 10.* Guanidine nitrate (0·2M at 25°) in perchloric acid (60·8%, w/w).
Equil. val. : $[HNO_3]$, 0·158M

t	18	30	60	96	150	240
$[HNO_3]$	0·1872	0·1823	0·1780	0·1724	0·1653	0·1604
t	360	540	710 *	840 *	1100 *	
$[HNO_3]$	0·1582	0·1578	0·1573	0·1572	0·1563	

Expts. 11, 12.* Nitroguanidine (0·2M at 25°) in perchloric acid (60·8%, w/w),
Equil. val. : $[HNO_3]$, 0·158M.

t	9	21	36	58	88	143
$[HNO_3]$	0·0073	0·0173	0·0308	0·0467	0·0674	0·0972
t	215	320	566	736 *	916 *	1083 *
$[HNO_3]$	0·1217	0·1423	0·1548	0·1573	0·1570	0·1564

* Asterisks relate values of t to experiment numbers similarly marked.

Nitration of Acetanilide by Means of Nitrourethane or Nitroguanidine in Selenic Acid.—Nitrourethane or nitroguanidine (2·5 m.-mol.) was added during 20 min. at 25° to a stirred solution of acetanilide (2·5 m.-mol.) in selenic acid (2·5 ml. of 91·0%, w/w). After 20 min. at 25°, the solution was poured on ice (35 g.) to yield *p*-nitroacetanilide, m. p. 211°. The yield from nitrourethane was 74%; from nitroguanidine, 50%; from potassium nitrate (control), 75%.

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[*Received April 11th*, 1953.]