CCCXXIX.—*The Interaction of Bromine with Acetic Anhydride. Part II.*

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IT has been stated by Orton and Jones (J., 1912, **101**, 1722), and subsequently by W. H. Gray (Thesis, Univ. of Wales, 1913) and by Orton, Watson, and Bayliss (Part I, J., 1923, **123**, 3081), that pure acetic anhydride is unattacked by halogens at the ordinary temperature when light is completely excluded. The anhydride used by these investigators was obtained by fractional distillation of Kahlbaum's acetic anhydride "free from homologues," and their observation does not appear to find confirmation in the results of earlier workers (Gal, *Ann. Chim. Phys.*, 1862, **66**, 187; Urech, *Ber.*, 1880, **13**, 1687; Lapworth, J., 1904, **85**, 40). The stability to bromine of specimens of acetic anhydride of varied origin and purified by different methods has now been examined; in every case reaction occurs, and it appears probable that the material employed by the previous workers contained a trace of some inhibitor which was not removed by fractionation. A search for possible inhibitors has revealed the fact that introduction of quinoline in minute quantity prevents the reaction from proceeding to any perceptible extent during a long interval of time (with bromine = $0{\cdot}25M$ and quinoline = $0{\cdot}006M$, no measurable amount of bromine reacted in 93 hrs.); moreover, acetic anhydride containing a trace of quinoline is still stable to bromine after fractionation. After this "latent period," reaction proceeds at a measurable rate, but the disappearance of bromine is much slower than when pure anhydride is employed; the retardation at this stage is probably to be attributed to the presence of a hydrobromide of quinoline, for a similar retardation is produced by introduction of a trace of sodium or potassium bromide or of certain other salts. Sodium acetate exerts an influence which is similar to but not as powerful as that of quinoline (with $Br_2 = 0{\cdot}26M$ and $NaC_2H_3O_2 = 0{\cdot}005M$, no fall of titre after 17 hrs.), whilst pyridine, dimethylaniline, triethylamine, diethylamine, *iso*quinoline, ammonium acetate, methylamine, and ethylamine are less effective. Addition of a trace of nitric acid or of acetyl nitrate is accompanied by an extremely powerful inhibition (compare Gray, *loc. cit.*); the effect of the former is probably due to acetyl nitrate formed by reaction of the nitric acid with the anhydride, for the bromination of propionic anhydride (which is similar to that of acetic anhydride, but considerably slower) is inhibited by acetic anhydride and nitric acid in conjunction, but not by nitric acid alone.

The speed of interaction of bromine with acetic anhydride is now found to be greatly influenced by the concentration of the halogen. The course of the reaction indicates autocatalysis, and introduction of acetyl bromide (one of the products, Gal, Urech, *locc. cit.*) causes a considerable acceleration. The effect of acetyl bromide is identical with that of hydrogen bromide at equimolar concentration, indicating that the halogen acid reacts all but completely with the anhydride, $(CH_3{\cdot}CO)_2O + HBr = CH_3{\cdot}COBr + CH_3{\cdot}CO_2H$, as has been shown by an aspiration method. Introduction of propionyl or benzoyl bromide brings about an acceleration identical with that produced by acetyl bromide at the same concentration. These facts recall the bromination of carboxylic acids (Watson, J., 1925, **127**, 2067), and a similar series of changes of the following type is indicated :

$$CH_3{\cdot}COBr + Br_2 = CH_2Br{\cdot}COBr + HBr \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$(CH_3{\cdot}CO)_2O + HBr \rightleftarrows CH_3{\cdot}COBr + CH_3{\cdot}CO_2H \quad . \quad . \quad . \quad . \quad (2\text{A})$$

$$(CH_3{\cdot}CO)_2O + CH_2Br{\cdot}COBr \rightleftarrows CH_2Br{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CH_3 + CH_3{\cdot}COBr \quad . \quad . \quad . \quad (2\text{B})$$

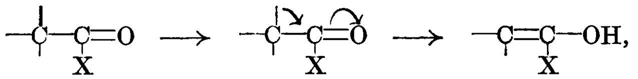
$$CH_3{\cdot}CO_2H + CH_2Br{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CH_3 \rightleftarrows (CH_3{\cdot}CO)_2O + CH_2Br{\cdot}CO_2H \quad . \quad . \quad . \quad . \quad (3)$$

When the bromide of another acid is added initially, these reactions will be preceded by

$$(CH_3{\cdot}CO)_2O + R{\cdot}COBr \rightleftarrows CH_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}R + CH_3{\cdot}COBr, \text{ or}$$
$$(CH_3{\cdot}CO)_2O + 2R{\cdot}COBr \rightleftarrows (R{\cdot}CO)_2O + 2CH_3{\cdot}COBr \quad . \quad . \quad (4)$$

That acetic anhydride can react with acid bromides in this manner is demonstrated by distilling a quantity of the anhydride with either bromoacetyl or benzoyl bromide, whereby a good yield of acetyl bromide is obtained; it is not suggested that reaction (3), which is analogous to the reactions of acids with anhydrides observed by Kaufmann and Luterbacher (*Ber.*, 1909, **42**, 3483), proceeds to any great extent under the conditions of the authors' experiments, in which the acetic anhydride was always in great excess. In the above series of reactions the rate of disappearance of bromine will be $dx/dt = k(a-x)[\text{AcBr}]$, where a is the initial concentration of bromine. If the acetyl bromide be present in excess, the reaction will be of the first order; values of $k_1 = 1/t \, . \log_e a/(a - x)$, however, were not constant. If the bromine also reacts with the enolic form of the anhydride (this form being produced slowly and reacting with halogens rapidly; compare Part I), the rate of disappearance of bromine will be $dx/dt = k(a - x)[\text{AcBr}] + k'[\text{Ac}_2\text{O}]$, where x is the total amount of the halogen which reacts in time t. In the case when both acid bromide and anhydride are in excess, this reduces to $dx/dt = C(a - x) + C' = C(a - x + P)$, where $C' = CP$, which on integration becomes $C = 1/t \, . \log_e (a + P)/(a + P - x)$. Constant values of C were obtained by use of this expression. The observed facts are thus interpreted by supposing that the reaction proceeds mainly through a series of changes involving the bromination of the acid bromide, but also to a small extent through the enolised anhydride. Addition of a small quantity of sulphuric acid, ferric chloride,* or stannic chloride results in a marked increase in the rate of disappearance of bromine (compare Part I); their effect probably consists in an acceleration of the enolisation of the anhydride. Acetyl chloride (or added hydrogen chloride), trichloroacetic acid, and monobromoacetic acid are without appreciable effect. When pure anhydride is used, pure dry iodine is now found to be a catalyst, but iodine bromide (added as such) and iodine chloride are more effective, the former being a particularly good catalyst.

According to the hypothesis of activation by electronic displacement (Allan, Oxford, Robinson, and Smith, J., 1926, 401; Ingold and Ingold, *ibid.*, p. 1310) there will be but little tendency for a proton to become loosened from the methyl group of acetic acid, for the carboxyl group is " self-contained " (Ray and Robinson, J., 1925, **127**, 1618); adjustment of the covalencies of the carbonyl carbon atom of acetic anhydride, however, will take place to a smaller extent, since the singly-linked oxygen is conjugated on both sides (compare Lea and Robinson, J., 1926, 411), whilst with acetone and acetyl bromide no such adjustment is possible. In the three compounds last mentioned, therefore, loosening of a proton will occur, and will be most marked in acetyl bromide owing to the " polar effect " of the bromine atom (Baker and Ingold, J., 1926, 2466). The loosened proton is attracted towards the negatively charged carbonyl oxygen, and enolisation takes place (in preference to direct substitution by a reagent, as is shown by the dynamics of the bromination of acetone; Lapworth, *loc. cit.*). The sequence $CH_3{\cdot}COBr > (CH_3)_2CO > (CH_3{\cdot}CO)_2O > CH_3{\cdot}CO_2H$ is thus obtained for velocity of enolisation. The series of changes up to this point may be written



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* Using pure anhydride, the authors have failed to confirm the violet colour ascribed in Part I (p. 3090) to solutions of anhydrous ferric chloride. Such solutions are brown in colour.

and on activation of the enolide

$$-\underset{|}{C}=\underset{\substack{|\\X}}{C}-OH \longrightarrow -\underset{\substack{|\\\ominus}}{C}=\underset{\substack{|\\X}}{C}-\underset{\oplus}{O}H.$$

The activated enolide will react with bromine at the negatively charged carbon atom, the products being the monobrominated ketonic derivative and hydrogen bromide. In acetyl bromide, the activation of the enolide will be opposed by the polar effect of the bromine atom, and hence *rapid* enolisation will be followed by a comparatively slow reaction with bromine (compare Watson, *loc. cit.*, p. 2075), whilst in acetone and acetic anhydride slow enolisation is followed by rapid reaction with the halogen. These considerations lead to the idea suggested originally by Lapworth (*loc. cit.*) that the bromination of carbonyl compounds in general is preceded (provided an α-hydrogen atom is present) by conversion into the enolic form; it is not necessary, however, to assume the formation of an intermediate dibromide which immediately loses hydrogen bromide, nor has such a dibromide been isolated. This scheme correlates the results of Lapworth and others on the bromination of ketones and aldehydes, those of Watson on the bromination of carboxylic acids, and also those described in the present paper.

EXPERIMENTAL.

The velocity measurements were carried out by withdrawal at suitable intervals of 2 (± 0·01) c.c. of the reaction mixture, addition to aqueous potassium iodide, and titration of the iodine liberated with $N/10$-thiosulphate. Unless otherwise stated, titres are expressed as c.c. of $N/10$-thiosulphate, and time in minutes. Temperature throughout = 25°.

Reaction of Bromine with Different Specimens of Acetic Anhydride.—The anhydride was fractionated through an eight-pear stillhead, and the bromine (B.D.H. " A.R." quality) was purified as described by Watson (*loc. cit.*, p. 2076).

Br_2 = 0·25—0·27M, initially; mol. ratio Ac_2O/Br_2 = 40.

	Fall in titre after (mins.)							
Initial titre.	20.	30.	40.	50.	60.	70.	80.	90.
Kahlbaum's acetic anhydride " free from homologues " (post-war).								
10·30	1·45	2·80	4·52	5·90	7·10	8·05	8·72	9·20
Hopkin and Williams's " Reagent " acetic anhydride (post-war). (Mean of results for ten specimens.)								
10·38 (±0·25)	1·32	2·65	4·00	5·42	6·65	7·20	8·38	8·98 (±0·5)
British Drug Houses " A.R." acetic anhydride (post-war).								
10·45	1·70	3·45	4·85	6·32	7·60	8·42	9·05	9·48

Effect of Purification of Bromine.—Method 1 as above : results are the mean of those in previous table. Method 2 : bromine distilled from potassium bromide and zinc oxide (compare Stas, *Mem. Acad. Belgique*, 1865, **35**, 3; West, J., 1924, **125**, 1279), then dried over quick-lime and distilled in an all-glass apparatus. Method 3 : bromine distilled from potassium bromide and zinc oxide, then washed with distilled water and dried under concentrated sulphuric acid, separated, and distilled from a little barium carbonate.

	Initial titre.	Fall in titre after (mins.)							
		20.	30.	40.	50.	60.	70.	80.	90.
Method 1 ...	10·38	1·48	2·98	4·45	5·62	7·12	7·88	8·72	9·22
Method 2 ...	10·40	1·10	2·28	3·65	5·12	6·35	7·35	8·20	8·82
Method 3 ...	10·28	0·90	1·80	3·05	4·55	5·75	6·85	7·75	8·45
Untreated ...	10·15	1·35	2·70	4·22	5·70	6·82	7·78	8·45	9·00

Effect of Purification of Acetic Anhydride by Different Methods.—Specimens of the anhydride were distilled from phosphorus pentoxide (method 1), potassium permanganate (2), or chromic anhydride (3); allowed to stand for 48 hours over pure anhydrous sodium acetate and then distilled (4), refluxed for 12 hours over sodium acetate and then distilled (5), and treated with 0·1% by volume of bromine, allowed to stand until colourless, refluxed for 6 hours over sodium acetate, and distilled (6). In each case, the anhydride was fractionated both before and after the treatment described.

	Initial titre.	Fall in titre after (mins.)							
		20.	30.	40.	50.	60.	70.	80.	90.
Method 1 ...	10·52	1·42	3·60	5·25	6·68	7·78	8·60	9·20	9·60
Method 2 ...	10·55	1·05	2·28	3·78	5·20	6·55	7·60	8·40	9·10
Method 3 ...	10·45	1·38	3·02	4·65	6·05	7·25	8·22	8·92	9·40
Method 4 ...	10·50	1·70	3·25	4·80	6·45	7·60	8·52	9·12	9·55
Method 5 ...	10·45	1·68	3·05	4·65	6·08	7·22	8·12	8·80	9·30
Method 6 ...	10·25	1·60	3·25	4·88	6·20	7·95	8·22	8·50	9·30

Effect of varying Bromine Concentration.

Conc. of bromine.	Initial titre.	Fall of titre after (mins.)							
		20.	30.	40.	50.	60.	70.	80.	90.
0·474*M*	18·95	6·75	11·28	14·18	16·12	17·32	18·10		
0·260*M*	10·38	1·48	2·98	4·45	5·62	7·12	7·88	8·72	9·22
0·148*M*	5·92	0·35	0·70	1·10	1·68	2·28	2·82	3·38	3·85

Effect of Inhibitors.—The substances used were the purest specimens obtainable, further purified in many cases by the usual methods.

Substance added.	Conc. (M) (±0·001).	Initial titre.	Time (mins.) required for fall in titre of		
			2 c.c.	6 c.c.	9 c.c.
Quinoline	0·006	10·25	6960	7080	7320
Sodium acetate	0·005	10·55	1200	1320	1530
„ „	0·0025	10·42	555	630	795
„ „	0·0005	10·25	45	90	135
Pyridine	0·005	12·75	495	585	630
Dimethylaniline	0·005	9·82	255	495	735
Triethylamine	0·005	10·75	165	375	660
Diethylamine	0·005	10·35	105	210	360
*iso*Quinoline	0·009	10·12	90	315	—
Ammonium acetate	0·005	10·45	60	105	150
Methylamine	0·005	10·30	60	135	240
Ethylamine	0·005	10·42	45	105	195
Sodium bromide	0·005	10·15	285	525	840
Potassium bromide	0·0055	10·35	240	480	780
Sodium chloride	Trace	10·35	180	510	900
Sodium benzenesulphonate	„	10·25	60	120	300

Effect of Nitric Acid and of Acetyl Nitrate.—A solution of pure nitric acid (prepared from pure potassium nitrate and pure sulphuric acid) in acetic acid (m. p. 16·4°) was freed from nitrous acid by aspiration with purified air (Gray, *loc. cit.*) and estimated in a Lunge nitrometer. 0·05 C.c. of this solution and 0·3 c.c. of bromine were made up to 25 c.c. at 25° with acetic anhydride, giving $HNO_3 = 0{\cdot}003M$. The titre of 2 c.c. of this solution was as follows :

Time (days)	0	3	5	7	10	17
Titre (c.c.)	10·55	10·40	10·40	10·25	9·95	9·55

0·1 C.c. of acetyl nitrate, prepared as described by Pictet and Khotinsky (*Compt. rend.*, 1907, **144**, 210), b. p. 27°/30 mm., and 0·3 c.c. of bromine were made up to 25 c.c. with acetic anhydride. Titre of 2 c.c. as follows :

Time (days)	0	14
Titre (c.c.)	11·38	11·15

Propionic anhydride, prepared by fractionation of Kahlbaum material (b. p. 166°/771·5 mm.), reacted with bromine as follows :

Time (hrs.)	0	2	3	5	7	10
Titre (c.c.)	9·32	9·12	8·18	7·75	7·10	6·40

With propionic anhydride, to which a little nitric acid (0·03M) had been added, a titre of 10·05 c.c. fell to 2·85 c.c. in 48 hours. When acetic anhydride (0·03M) and nitric acid (0·03M) were both added, a titre of 10·98 c.c. fell only to 10·95 c.c. in 5 days.

Effect of Catalysts and Other Substances.—Solutions of hydrogen bromide and hydrogen chloride in the anhydride, pure acetyl chloride, and pure acetyl, benzoyl, and propionyl bromides were obtained as described by one of us (Watson, *loc. cit.*). The sulphuric acid, ferric chloride, and stannic chloride were purified by distillation or sublimation, and pure iodine and iodine bromide were prepared as described in Part I, p. 3094.

Substance added.	Conc., *M*.	Initial titre.	Fall in titre after (mins.)						
			10.	20.	30.	40.	50.	60.	70.
AcBr	0·024	10·38	1·32	3·12	4·90	6·52	7·68	8·52	9·18
HBr	0·024	10·25	1·45	3·25	5·15	6·58	7·68	8·55	9·15
BzBr	0·024	10·40	1·42	3·32	5·18	6·75	7·82	8·65	9·30
AcBr	0·109	11·30	2·88	5·52	7·48	8·92	9·80	10·40	
PrBr	0·109	11·50	2·92	5·62	7·62	9·02	9·92	10·58	
BzBr	0·109	11·10	2·78	5·45	7·38	8·78	9·70	10·22	
AcBr	0·240	10·28	3·52	6·32	8·05	9·00	9·65		
HBr	0·240	9·90	3·68	6·35	7·95	8·85	9·40		
HCl	0·027	10·10	0·38	1·25	2·92	4·50	5·85	7·05	7·95
HCl	0·270	10·15	0·50	1·55	3·25	4·85	6·20	7·35	8·25
HCl	0·540	10·28	0·58	1·82	3·35	5·08	6·50	7·60	8·35
AcCl	0·270	10·15	0·25	1·25	2·88	4·42	5·85	7·02	7·85
AcCl	0·540	10·22	0·75	1·72	3·10	4·68	6·02	7·08	8·08
$CCl_3\cdot CO_2H$	0·009	10·50	0·45	1·40	2·95	4·70	6·15	7·40	8·22
$CCl_3\cdot CO_2H$	0·048	10·25	0·40	1·32	2·85	4·52	5·92	7·10	8·00
$CH_2Br\cdot CO_2H$	0·147	10·40	0·50	1·65	3·10	4·85	6·15	7·38	8·22
$CH_3\cdot CO_2H$	0·450	10·12	0·38	1·80	3·30	5·10	6·58	7·52	8·40
H_2SO_4	0·001	10·30	1·00	2·95	5·15	6·78	8·18	9·18	9·82
H_2SO_4	0·002	10·20	1·28	3·40	5·75	7·55	8·98		

Substance added.	Conc., *M*.	Initial titre.	Fall in titre after (mins.)					
			10.	15.	20.	25.	30.	35.
$FeCl_3$	0·0012	10·22	1·25	2·68	4·45	6·10	7·85	9·08
$FeCl_3$	0·0024	10·40	3·18	6·50	9·40	10·22		
$SnCl_4$	0·0029	10·18	0·78	1·60	3·38	5·40	7·70	9·20
I_2	0·0030	10·02	1·72	3·92	6·15	8·22	9·75	9·95
I_2	0·0060	9·95	3·98	7·60	9·82			
IBr	0·0006	10·40	2·00	3·90	6·25	8·42	9·80	
IBr	0·0012	10·25	3·80	6·90	9·15	10·00		
IBr	0·0060	9·55	9·52					
ICl	0·0006	10·28	0·65	1·42	2·50	3·82	5·28	6·68
ICl	0·0060	10·32	5·10	9·85				

Examination of a Solution of Hydrogen Bromide in Acetic Anhydride.—The solution was prepared in the same way as those employed in the velocity measurements. A known volume was placed in a bubbler standing in a thermostat at 25°, and a measured volume of pure, dry air was aspirated through this solution and then into standard alkali; the excess of alkali was determined by titration, and the bromide estimated as silver bromide. The amounts of acetic anhydride and acetic acid aspirated over were obtained by blank experiments under identical conditions, the proportion of acetic acid in the mixture being calculated from the equation $HBr + (CH_3\cdot CO)_2O = CH_3\cdot COBr + CH_3\cdot CO_2H$. If the vapour aspirated into the alkali contained acid bromide and no hydrogen bromide, the results would give Mols. acid/Mols. bromide = 2. The mean of two experiments was as follows: Conc. of HBr = 1·41*M*. 500 C.c. of air aspirated through 35 c.c. of this solution in 10 mins. Alkali neutralised = 21·20 c.c. of *N*/20, Alkali equivalent to Ac_2O and HAc aspirated over = 4·95 c.c. (from blank expt.). Alkali equivalent to HBr or AcBr aspirated over = 16·25 c.c. Wt. of AgBr = 0·0766 g. Hence, mol. acid aspirated over = 0·000812, and mol. bromide = 0·000407. Mol. acid/mol. bromide = 1·99. Applied to other similar solutions, the method gave the following results: Solution of acetyl chloride in acetic anhydride, mol. acid/mol. chloride = 1·98; solution of hydrogen chloride in acetic acid, mol. acid/mol. bromide = 0·98.

Reaction of Acetic Anhydride with Acid Bromides.—Acetic anhydride and bromoacetyl bromide in molar proportion were slowly distilled in an all-glass apparatus; a considerable quantity of liquid distilled at 76—79°/760·9 mm.; this fraction was added to water and the bromine precipitated as silver bromide, giving Br, 63·75 (calc. in AcBr: Br, 65·04%); a smaller fraction distilled at 137—138°, smelt strongly of acetic anhydride, and was probably a mixture of the anhydride with unchanged bromoacetyl bromide (%Br as COBr, 26·05; %Br as COBr in bromoacetyl bromide, 39·6). A fraction of high b. p. remained, probably $(CH_2Br{\cdot}CO)_2O$, which is formed when the mixed anhydride, $CH_2Br{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CH_3$, is distilled (Naumann, *Annalen*, 1864, **129**, 273). Benzoyl bromide (2 mols.) was distilled with acetic anhydride (1 mol.); a large fraction, collected at 77—82°/775 mm., gave %Br as COBr, 65·36; from the liquid remaining some benzoic anhydride (m. p. 40°) and benzoic acid were obtained.

Reaction of Bromine with Acetic Anhydride and Excess of Acetyl Bromide.—In both experiments, $Ac_2O = 9{\cdot}067M$, $AcBr = 1{\cdot}898M$, $P = 0{\cdot}01125$. Titre in c.c. of $N/50$-thiosulphate.

I. $a = 0{\cdot}0887M$.			II. $a = 0{\cdot}0294M$.		
Time.	Titre.	C.	Time.	Titre.	C.
0	17·75		0	5·88	
3	13·35	0·0827	6	2·80	0·0793
7	9·10	0·0808	9	1·70	0·0801
9	7·45	0·0803	14	0·35	0·0813
16	3·32	0·0798			
		Mean 0·0809			Mean 0·0802
		$k = 0{\cdot}0426$			$k = 0{\cdot}0423$

Average value of $k = 0{\cdot}04245$, giving $C' = 0{\cdot}000906$, $k' = 0{\cdot}0001$.

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