380. *The Labile Nature of the Halogen Atom in Organic Compounds. Part XV. The Action of Hydrazine on Bromomalonic Esters.*

By H. P. Gallus and A. Killen Macbeth.

The positive character of the halogen atom in bromomalonic esters expresses itself in the oxidation of hydrazine hydrate, and measurement of the nitrogen liberated provides a method for determining the extent to which the reaction proceeds. The rate of reaction is greatly decreased in the case of the higher esters, those of the primary alcohols requiring up to 15 minutes for liberation of the final volume of nitrogen. The time is still greater with esters of the secondary alcohols, and the oxidation is not quantitative.

The isolation of the *hydrazone* of mesoxalhydrazide when *iso*butyl and *iso*amyl dibromomalonates are treated with hydrazine hydrate indicates that, although hydrolysis involving the replacement of bromine by hydrogen is the main reaction, the alternative course in which the halogen is replaced by hydroxyl is also followed to some extent.

In previous parts of this series it was shown that the halogen atom in compounds such as the halogenated derivatives of nitroparaffins, malonic esters, and certain 1 : 3-diketo-compounds presented marked differences in reactivity from that in, *e. g.*, picryl chloride, acyl halides, and sulphonyl chlorides. In the former type of compound, alternate polarity effects, with the negative oxygens as key atoms, would lead to an induced positive effect on the halogen atoms. The reactivity of such atoms expresses itself in the oxidation of hydrazine hydrate, and the reaction may be followed quantitatively by measurement of the liberated nitrogen, a behaviour which readily differentiates the negative halogen of acyl halides and other compounds, in which hydrazide formation, without oxidation, occurs.

A corollary to the induced positive effect is a difference in reactivity between (1) chlorine and bromine in similarly constituted compounds (Macbeth and Traill, J., 1925, **127**, 1119) and (2) the same halogen in compounds of diverse structure (Macbeth and co-workers, J., 1922, **121**, 1120, 2176; 1923, **123**, 1129; 1926, 1248).

The reduction of the bromomalonic esters by hydrazine is expressed in the following equations, which do not, however, take into account hydrazide formation at the ester groups:

$$CBr_2(CO_2R)_2 + NH_2{\cdot}NH_2 = CH_2(CO_2R)_2 + N_2 + 2HBr$$
$$2CHBr(CO_2R)_2 + NH_2{\cdot}NH_2 = 2CH_2(CO_2R)_2 + N_2 + 2HBr$$

Hirst and Macbeth (J., 1922, **121**, 904) found that, whereas ethyl bromomethylmalonate reacted completely with hydrazine hydrate in a few minutes at laboratory temperature, there was a remarkable decrease in the rate of reaction with the higher homologues; and in these the theoretical amount of nitrogen for complete reduction was not liberated. It was suggested that the low results might be due to the presence of dialkyl-substituted malonates (cf. Fischer, *Ber.*, 1906, **39**, 351), and that the decrease in the rate of reaction might be attributed to steric effects of the substituents. A series of bromo- and dibromo-malonic esters, in which the ester groups are varied, has now been examined. A decrease in the rate of reaction and in the yield of nitrogen is found as the complexity of the ester groups increases; *e.g.*, under the experimental conditions, the bromomalonates behave as follows: the methyl ester gives off the theoretical amount of nitrogen in about 1·75 minutes, the esters of all other primary alcohols require 5—15 minutes, but the volume of nitrogen is somewhat deficient, and those of secondary alcohols require at least 50 minutes and give off much less gas.

Hydrolysis of halogen compounds may follow either of two courses, the halogen being replaced by hydrogen and the solution acquiring oxidising properties, or the halogen being replaced by hydroxyl, and it is probable that cases in which a deficiency of nitrogen is liberated may be accounted for by the occurrence of the second type of reaction to some extent. This, in the case of a dibromomalonic ester, would lead to the formation of mesoxalic acid, which would be isolated as the *hydrazone* of *mesoxalhydrazide*, and we have actually obtained this hydrazone from the reaction of the *iso*amyl and the *iso*butyl ester with hydrazine hydrate in alcoholic solution. Moreover, we have confirmed the work of Ruhemann and Orton (J., 1895, **67**, 1003), who similarly obtained the hydrazone of mesoxalamide from hydrazine hydrate and dibromomalonamide. Whether or not the course of the former reaction is influenced by the ease of conversion of a particular ester into the hydrazide as a first step cannot yet be answered, but evidence on this point is being sought.

EXPERIMENTAL.

Preparation of Malonic Esters.—These were prepared either (i) by the simultaneous hydrolysis and esterification of sodium cyanoacetate in the presence of the desired alcohol and sulphuric acid, or (ii) by the direct esterification of malonic acid in the presence of excess of alcohol to ensure the formation of the di-ester. In the former method, olefin formation was reduced by adding the sulphuric acid drop by drop during refluxing; and with the same object in view the acid was added in two portions in direct esterification, one-half at the beginning of the reaction and the remainder some 3 hours later when, in the case of the higher alcohols, the liquid showed separation into two layers—with the lower alcohols, on account of their solubilities, such separation does not occur. By this procedure increased yields were obtained, *sec.*-octyl, *cyclo*hexyl, and 2- and 3-methyl*cyclo*hexyl alcohols giving ester in yields of 94, 59, 74, and 69% instead of 70, 44, 60, and 60% respectively. The following malonates were prepared: *n*-Propyl, b. p. 223—225°; *n*-butyl, b. p. 130—131°/12 mm.; *n*-amyl, b. p. 130°/6 mm. (Found: C, 63·8; H, 9·8. Calc.: C, 63·9; H, 9·9%); n-*octyl*, b. p. 176—177°/6 mm. (Found: C, 69·4; H, 11·1. $C_{19}H_{36}O_4$ requires C, 69·4; H, 11·05%); *iso*propyl, b. p. 102°/23 mm. (Found: C, 57·1; H, 8·5. Calc.: C, 57·4; H, 8·6%); *iso*butyl, b. p. 129°/21 mm. (Found: C, 60·6; H, 9·2. Calc.: C, 61·1; H, 9·3%); *iso*amyl, b. p. 144—146°/12 mm.; *sec.*-octyl, b. p. 168—169°/4 mm.; cyclo*hexyl*, b. p. 173°/10 mm. (Found: C, 67·0; H, 8·95. $C_{15}H_{24}O_4$ requires C, 67·2; H, 9·0%); 2-*methyl*cyclo*hexyl*, b. p. 172—173°/10 mm. (Found: C, 68·5; H, 9·5. $C_{17}H_{28}O_4$ requires C, 68·9; H, 9·5%); 3-*methyl*cyclo*hexyl*, b. p. 178°/13 mm. (Found: C, 68·7; H, 9·6%); 4-*methyl*cyclo*hexyl*, b. p. 168°/10 mm. (Found: C, 68·5; H, 9·6%).

Method (i) proved unsatisfactory for the preparation of the *cyclo*hexyl and methyl*cyclo*hexyl esters. Attempts to prepare *tert.*-butyl malonate by this method or by direct esterification using hydrogen chloride or sulphuric acid as catalyst were unsuccessful. Hydrogen chloride was also unsatisfactory in the preparation of *iso*propyl malonate, the yield being only some 22%, and considerable quantities of β-chloropropane being formed.

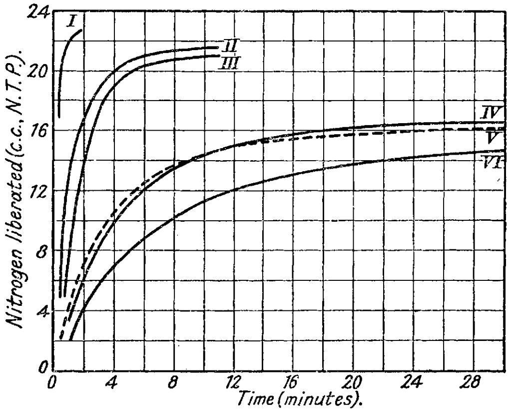
Preparation of Bromomalonic Esters.—The bromo-esters were prepared by the dropwise addition of excess of bromine to the previously warmed ester; the reaction proceeded in diffuse daylight, but was completed in the case of the dibromo-esters in direct sunlight. The mixture was then heated on a water-bath (to remove further hydrogen bromide), cooled, and washed successively with water, dilute sodium carbonate solution, and water. After drying, the product was fractionated. The following bromo-esters were prepared: Methyl bromomalonate, b. p. 110—112°/15 mm.; methyl dibromomalonate, m. p. 65° from light petroleum; *n*-propyl bromomalonate, b. p. 110—112°/8 mm. (Found: Br, 30·0. Calc.: Br, 29·9%); *n*-propyl dibromomalonate, b. p. 118°/6 mm. (Found: Br, 46·1. Calc.: Br, 46·2%); *iso*propyl bromomalonate, b. p. 86°/4 mm. (Found: Br, 29·4%); *iso*propyl dibromomalonate, b. p. 104°/6 mm. (Found: Br, 46·0%); n-*butyl bromomalonate*, b. p. 135—136°/10 mm. (Found: Br, 27·6. $C_{11}H_{19}O_4Br$ requires Br, 27·1%); n-*butyl dibromomalonate*, b. p. 147°/10 mm. (Found: Br, 42·6. $C_{11}H_{18}O_4Br_2$ requires Br, 42·8%); iso*butyl bromomalonate*, b. p. 124—126°/12 mm. (Found: Br, 27·25%); iso*butyl dibromomalonate*, b. p. 138°/10 mm. (Found: Br, 42·6%); n-*amyl bromomalonate*, b. p. 144°/6 mm. (Found: Br, 24·2. $C_{13}H_{23}O_4Br$ requires Br, 24·8%); iso*amyl bromomalonate*, b. p. 146—148°/11 mm. (Found: Br, 24·6%); iso*amyl dibromomalonate*, b. p. 142—143°/4 mm. (Found: Br, 38·7. $C_{13}H_{22}O_4Br_2$ requires Br, 39·8%); sec.-*octyl bromomalonate*, b. p. 169—170°/4 mm. (Found: Br, 19·7. $C_{19}H_{35}O_4Br$ requires Br, 19·7%); cyclo*hexyl bromomalonate*, b. p. 167°/4 mm. (Found: Br, 22·6. $C_{15}H_{23}O_4Br$ requires Br, 23·0%). In 2-, 3-, and 4-methyl*cyclo*hexyl bromomalonates, b. p. 176°/6 mm., 182°/6 mm., and 180—181°/4 mm., respectively, the bromine found was more than 1% lower than the 21·3% required.

Action of Hydrazine Hydrate.—The estimations of nitrogen liberated by the action of the bromo-esters on hydrazine hydrate (50% solution) were carried out in a van Slyke nitrometer.

0·01 G.-mol. of the monobromo-esters or 0·005 g.-mol. of the dibromo-esters was made up to 25 c.c. with absolute alcohol; 5 c.c. of this solution were washed into the reaction vessel with 10 c. c. of absolute alcohol, and vigorous shaking by an electric motor started. The shaking was temporarily stopped by braking whilst 2 c.c. of hydrazine hydrate (50%) were run in from the burette. This ensured the immediate vigorous shaking found necessary for concordant results, which were reproducible within 0·5—1%. The nitrogen liberated was collected over absolute alcohol. The final volumes, after allowance for vapour tension and reduction to *N.T.P.*, are shown above. Complete reduction requires the liberation of 22·4 c.c. of nitrogen at 0° and 760 mm.

	Bromo-malonates.	N_2 (c.c., *N.T.P.*).	Temp.	Time of reaction, mins.
Primary.	Methyl	22·35	23°	1·75
	n-Propyl	20·5	23	7
	n-Butyl	20·9	23	6·5
	n-Amyl	19·9	13	13·5
	n-Octyl	17·15	20	12
	*iso*Butyl	20·7	23	11
	*iso*Amyl	21·25	23	11
Secondary.	*iso*Propyl	16·7	23	65
	sec.-Octyl	15·8	23	75
	*cyclo*Hexyl	16·05	23	50
	2-Methyl*cyclo*-hexyl	14·5	14	120
	3-Methyl*cyclo*-hexyl	14·7	19	60
	4-Methyl*cyclo*-hexyl	15·7	16	150

Dibromo-malonates.	N_2 (c.c., *N.T.P.*).	Temp.	Time of reaction, mins.
Methyl	23·0	23°	2
Propyl	21·2	15	9
Butyl	22·0	17	6·5
*iso*Butyl	21·6	17	9·5
*iso*Amyl	20·5	20	9
*iso*Propyl	17·3	20	60



Reaction of Bromomalonic Esters with Hydrazine Hydrate at 23°.

I. *Methyl ester;* II. iso*Amyl ester;* III. iso*Butyl ester;* IV. iso*Propyl ester;* V. cyclo*Hexyl ester;* VI. sec-*Octyl ester.*

The above figures show that in all the cases examined other than the simple methyl ester, the nitrogen evolved falls somewhat short of the amount required for complete reduction, and the time of reaction also increases. This is especially marked with the esters of secondary alcohols. The progressive liberation of nitrogen at 23° was examined, and typical results are recorded in the graphs. These also show the difference between bromo-esters derived from primary and from secondary alcohols.

Hydrazone of Mesoxalhydrazide.—An excess of hydrazine hydrate (50%), when added to an alcoholic solution of *iso*butyl dibromomalonate, caused an energetic exothermic reaction to take place, nitrogen being freely evolved. When the liberation of gas ceased, the mixture was heated for a short time on the water-bath. Silky white needles separated on cooling, and when twice recrystallised from hot water had m. p. 187° (Found: N, 52·8. $C_3H_8O_2N_6$ requires N, 52·2%); a similar product (m. p. and mixed m. p.) was obtained from *iso*amyl dibromomalonate. It is evidently the ***hydrazone*** of ***mesoxalhydrazide***, and its isolation shows that to some extent the action of hydrazine hydrate on bromomalonic esters follows a course other than reduction.

JOHNSON CHEMICAL LABORATORIES, UNIVERSITY OF ADELAIDE.
[*Received, October 4th,* 1937.]