

ORGANIC FUNGICIDES. PART I. SYNTHESIS OF DIBROMOACETAMIDES

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Six new dibromoacetamides have been prepared preliminary to evaluation of their fungicidal activity. A new method for preparing dibromoacetic acid and dibromoacetyl chloride is given.

Strong fungicidal activity was observed by Weaver and Whaley (*J. Amer. Chem. Soc.*, 1947, **69**, 515) in some of the bromoacetanilides prepared in their laboratory. They synthesised a number of N-alkyl-bromoacetamides (*loc. cit.*) with a view to studying their fungicidal activity. The corresponding unhalogenated amides and the mono-halogenated paraffins were found to be non-toxic. The fungicidal activity of the bromoamides was therefore attributed to the position of the halogen atom.

The present work has been undertaken to study the modifications in fungicidal activity by increasing the number of halogen atoms in the molecule. It may be expected that such increase may possibly result in increased fungicidal activity as the halogen atom is supposed to be responsible for this property. With this aim in view, a number of analogous dibromoacetamides have been synthesised.

The starting material for the preparation of these amides is dibromoacetic acid. A survey of literature reveals that no satisfactory method is available for its preparation. So far it has been obtained by the action of excess of bromine on boiling acetic acid in the presence of sunlight, sulphur or phosphorus (Perkin and Duppa, *Annalen*, 1858, **108**, 111; Auwers and Bernhardt, *Ber.*, 1891, **24**, 2219; Genvresse, *Bull. Soc. chim.*, 1816, *iii*, **7**, 365). Carius (*Ber.*, 1870, **3**, 336) and Steiner (*Ber.*, 1874, **7**, 506) prepared it by the action of a large excess of bromine on ethyl acetate at 160°. In all these methods, much of the bromine is lost at the high temperature used and the dibromoacetic acid is obtained in low yields, the main product being monobromoacetic acid. Genvresse's method, which involves the heating of acetic acid and 5% sulphur with bromine at 150°, gives only 10% dibromoacetic acid. The present authors have prepared this acid in 88% yield by the decarboxylation of dibromomalonic acid.

The dibromoacetic acid has been converted into dibromoacetyl chloride by the action of thionyl chloride and the dibromoacetamides obtained by the action of different amines on the dibromoacetyl chloride in ether medium.

EXPERIMENTAL

Dibromoacetic Acid.—Dibromomalonic acid was first prepared by the action of bromine in chloroform on malonic acid according to the method of Patrieff (*Ber.*, 1874, **7**, 401). Bromine (165 g.) and chloroform (400 c.c.) were taken in a round bottomed flask fitted with a condenser, the latter being connected to an absorption tower. Finely powdered malonic acid (50 g.) was then added and the whole mass stirred. Gradually the reaction became brisk. The flask was then immersed in ice to control the reaction. When the reaction slowed down, the whole mass was left at room temperature (30°) for 24 hours. It was then refluxed on a water-bath till no more HBr evolved and the

mass was nearly decolorised. It was filtered and washed with chloroform. Dibromomalonic acid was obtained as colourless crystals, m. p. 131° , yield 110 g. (88% theory).

Dibromomalonic acid (110 g.) was decarboxylated at 130° in an oil-bath. The residual liquid was distilled under reduced pressure when a yellow liquid was obtained, b. p. 125° - $135^{\circ}/10$ mm., yield 80 g. (88% of theory). [Found: Br, 73.10; equiv. (neutralisation), 217.7. Calc. for $C_2H_2O_2Br_2$: Br, 73.36 per cent. Equiv., 217.8). This confirms that it is dibromoacetic acid.

Dibromoacetyl Chloride.—Thionyl chloride (80 c.c., 3 moles) was added dropwise to dibromoacetic acid (70 g., 1 mole) under constant stirring at 0° . A vigorous reaction took place and after the reaction had subsided, the mixture was left overnight. It was then refluxed on a water-bath for an hour, the excess of thionyl chloride removed and the residual liquid was distilled under reduced pressure, when it was obtained as an orange-yellow liquid, b. p. 60° - $64^{\circ}/4$ mm., yield 62 g. (82% of theory).

Dibromoacetamides.—Two molecular proportions of the required amine in 15 c.c. of dry ether were taken in a 250 c.c. flask, fitted with a dropping funnel and reflux condenser, and cooled in ice. Dibromoacetyl chloride (one molecular proportion), dissolved in 15 c.c. of dry ether was then added drop by drop. A vigorous reaction took place. The reaction mixture was left overnight and then the ether distilled off. The residual solid was a mixture of the amide and the amine hydrochloride. The latter was removed by treating with water and the remaining solid (amide) was then extracted with ether. The ethereal layer was separated, the ether removed and the compound was recrystallised from a suitable solvent. Most of them have an irritating action on the skin.

The following compounds have been obtained.

Dibromoacetamides.

Name of compounds.	M. p.	Yield.	Mol. formula.	% of Nitrogen found. required.	
1. N-Methyl dibromoacetamide	122°	84.6%	$C_3H_5ONBr_2$	5.85	6.06
2. N-Ethyl dibromoacetamide	81°	75.0	$C_4H_7ONBr_2$	5.75	5.72
3. N-n-Butyl dibromoacetamide	76°	86.0	$C_6H_{11}ONBr_2$	4.73	5.12
4. N-Diethyl dibromoacetamide	212°	49.0	$C_6H_{11}ONBr_2$	5.5	5.12
5. N-Dibromoacetanilide	138°	95.0	$C_9H_7ONBr_2$	4.13	4.8
6. N-Dibromoacetyl-phenyl- hydrazine	Does not melt, but decomposes above 200°	92	$C_9H_9ON_2Br_2$	8.85	9.09