Summary

A procedure is reported leading to the isolation of *o,o'*-DDT from technical DDT in amounts of about 0.1% of the original product. The method involved isolation of the DDT-isomer fractions by crystallization and chromatographic analysis and preferential dehydrochlorination of the more reactive DDT isomers, followed by oxidation of these products, leaving the unreactive *o,o'*-DDT.

The structure of *o,o'*-DDT has been proved by degradation.

A number of derivatives and compounds related to *o,o'*-DDT have been described.

The isolation of a degradation product, *m,p'*-dichlorobenzophenone, indicates the presence of *m,p'*-DDT in technical DDT.

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[CONTRIBUTION FROM THE CHEMISTRY DIVISION OF THE NAVAL RESEARCH LABORATORY]

Organic Fungicides. I. The Preparation of Some α-Bromoacetamides

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The synthesis of N-alkyl-α-bromoacetamides was undertaken because certain α-bromoacetanilides prepared in this Laboratory were found to be very fungicidal. It has been noted also that haloacylamides are claimed as seed disinfectants.[1] Since the unhalogenated amides and monohalogenated paraffins investigated were non-toxic, the fungicidal activity of α-bromo amides may be attributed to the position of the halogen, which is particularly reactive.

There is a surprising lack of information in the literature concerning these compounds. N-Ethyl-α-bromoacetamide has been reported as a product of hydrolysis from the corresponding imide chloride.[2] The N,N-diethyl compound has been prepared in 20% yield from diethylamine and bromoacetyl bromide.[3] The N-allyl derivative has been prepared in 85% yield by Bergmann, Dreyer and Radt[4] according to the method used by Harries[5] for the corresponding chloro compound. The rest of the compounds reported here are new.

Analytical results and physical properties of all the compounds prepared are given in Table I. All the monosubstituted amides were low-melting solids, while the disubstituted compounds were liquids as anticipated from well-known theories of association.[6] The properties of the bromoacetamides do not render them unsuitable for many fungicidal purposes. The lower liquid amides were sternutatory and lachrymatory, though not as markedly as the corresponding α-bromo esters. The other members exhibited these properties upon heating. It was not necessary to work in hoods and the compounds were only mildly irritating to the skin. The di-*i*-propyl and the di-*n*-butyl compounds were yellow liquids. The other compounds were white and have remained so for several months. The analytical data illustrate that several products were difficult to purify despite repeated distillations and alternate methods of preparation.

The standard practice of conducting acylations with acid halides in ether[7] has been discarded in favor of ethylene dichloride, which can be used without drying, is easily removed at reduced pressure without foaming, can be recovered for re-use, is inexpensive and apparently affords excellent yields. It is relatively non-inflammable and does not form explosive peroxides. This superiority of ethylene dichloride was pointed out by Wacker[8] and Seymour.[9]

Experimental

Reagents.—The bromoacetyl bromide, diethylamine, di-*n*-butylamine, allylamine and the amine hydrochlorides were obtained from Eastman Kodak Company, the *i*-propylamine and di-*i*-propylamine from Commercial Solvents Corporation, and the ethylene dichloride from Carbide and Carbon Chemicals Corporation. The other amines used were generously supplied by Sharples Chemicals, Inc. None of the reagents was purified before use.

Method Ia.—In a 500-cc., three-necked, round-bottomed flask equipped with a pentane thermometer, a dropping funnel and a mechanical stirrer were placed 150 cc. of ethylene dichloride and 0.2 mole of the amine. This solution was cooled to and maintained at −10° by a Dry Ice–ethanol bath while 0.1 mole of bromoacetyl bromide in 25 cc. of ethylene dichloride was added during a period of five to ten minutes. After stirring for five minutes longer, the mixture was filtered with suction to remove the crystallized amine hydrobromide. The filtrate was washed with several 25-cc. portions of very dilute hydrochloric acid and dried over anhydrous magnesium sulfate. After removal of the solvent by vacuum distillation (water-pump), the product was distilled at pressures obtainable with a mechanical pump.

Method Ib.—This method was the same as the first except that the filtrate was not washed due to the solubility of the lower members in water.

Method Ic.—This method was identical with Method Ia except that absolute ether was substituted for the ethylene dichloride. Commercial ether, when used as a solvent, contained sufficient ethanol to yield appreciable quantities of ethyl α-bromoacetate.

Method Id.—A solution of 0.2 mole of amine in 100 cc. of benzene was shaken in an ice-bath while 0.1 mole of

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[1] Maier-Bode, German Patent 695,907.

[2] von Braun, Jostes and Munch, *Ann.*, **453**, 113 (1927).

[3] Miller and Johnson, *J. Org. Chem.*, **1**, 135 (1936).

[4] Bergmann, Dreyer and Radt, *Ber.*, **54B**, 2139 (1921).

[5] Harries, *ibid.*, **43**, 634 (1910).

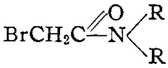
[6] Hantzsch, *ibid.*, **64**, 661 (1931); Buswell, Rodebush and Roy, THIS JOURNAL, **60**, 2444 (1938).

[7] Jacobs, Heidelberger and Rolf, *ibid.*, **41**, 458 (1919); Dehn, *ibid.*, **34**, 1399 (1912).

[8] Wacker, *Chem. Ztg.*, **45**, 266 (1920).

[9] Seymour, *J. Chem. Ed.*, **16**, 285 (1939).

TABLE I

α-BROMOACETAMIDES,

$BrCH_2C(=O)N(R)R'$

			Yield,	B. p.,[a]		M. p.[a]			MR			Nitrogen, %[i]		
R	R'	Method	%	° C.	Mm.	° C.	$n^{20}D$[b]	d^{20}_4[b]	Calcd.	Obs.	Formula	Calcd.	Found	
CH_3—	H—	IIa	61	61	0.6	44–45					C_3H_6BrNO	9.22	9.07	9.09
		IIb	43	122	20									
CH_3—	CH_3—	IIa	23	63–65	1.0	Liq.	1.5097	1.5412	32.20	32.20	C_4H_8BrNO	8.44	8.35	8.21
		IIb	32	115–116	18									
C_2H_5—	H—	IIa	82	72–77	0.3	47[c]					C_4H_8BrNO	8.44	8.35	8.23
		III	33	119–121	16–17									
C_2H_5—	C_2H_5—	Ib	67	82	0.6	Liq.[d]	1.4963	1.3745	41.44	41.25	$C_6H_{12}BrNO$	7.22	6.98	7.03
n-C_3H_7—	H—	Ia	75	70	0.3	*ca.* 20	1.4978	1.4455	36.82	36.49	$C_5H_{10}BrNO$	7.78	7.09	7.01[f]
		Ie	45	73–75	0.25								7.40	7.29
n-C_3H_7—	n-C_3H_7—	Ia	90	98	0.5	Liq.	1.4880	1.2686	50.68	50.42	$C_8H_{16}BrNO$	6.31	6.26	6.03
i-C_3H_7—	H—	Ib	86	70–72	0.8	66–67					$C_5H_{10}BrNO$	7.78	7.72	7.56
i-C_3H_7—	i-C_3H_7—	Ib	59	72–73	0.33	Liq.	1.4855	1.2651	50.68	50.34	$C_8H_{16}BrNO$	6.31	6.44	6.37
$CH_2=CH-CH_2$—	H—	Ib	76	90	0.6	*ca.* 25[e]					C_5H_8BrNO	7.87	7.35	7.24[g]
		Ie	41	87	0.35								8.28	8.14
n-C_4H_9—	H—	Ia	77	76	0.25	30–33					$C_6H_{12}BrNO$	7.22	6.97	7.05
		Ic	28	95	0.6									
n-C_4H_9—	n-C_4H_9—	Ia	90	101–102	0.22	Liq.	1.4840	1.2084	59.92	59.19	$C_{10}H_{20}BrNO$	5.60	5.59	5.64
		Id	62	102–105	0.3									
i-C_4H_9—	H—	Ia	83	99	0.3	37–40					$C_6H_{12}BrNO$	7.22	7.03	6.90
i-C_4H_9—	i-C_4H_9—	Ia	84	100	0.17	Liq.	1.4835	1.2016	59.92	59.47	$C_{10}H_{20}BrNO$	5.60	5.64	5.43
$CH_3CH_2CH(CH_3)$—	H—	Ia	85	83	0.4	53–54					$C_6H_{12}BrNO$	7.22	6.74	6.55[h]
		Ie	38	75–76	0.3								6.82	6.88
$CH_3CH_2CH(CH_3)$—	$CH_3CH_2CH(CH_3)$—	Ia	62	95	0.35	Liq.	1.4873	1.2073	59.92	59.63	$C_{10}H_{20}BrNO$	5.60	5.60	5.44
n-C_5H_{11}—	H—	Ia	82	107	0.5	*ca.* 25	1.4900	1.3108	46.06	46.01	$C_7H_{14}BrNO$	6.73	6.47	6.52
n-C_5H_{11}—	n-C_5H_{11}—	Ia	83	113	0.14	Liq.	1.4783	1.1091	69.16	71.05	$C_{12}H_{24}BrNO$	5.04	4.76	4.81
$CH_3CH_2CH_2CH(CH_3)$—	H—	Ia	87	100	1.5	*ca.* 30	1.4878	1.3019	46.06	46.04	$C_7H_{14}BrNO$	6.73	6.43	6.44
n-C_6H_{13}—	H—	Ia	83	99	0.3	*ca.* 25	1.4875	1.2617	50.48	50.68	$C_8H_{16}BrNO$	6.31	6.46	6.59
$CH_3CH_2CH(C_2H_5)CH_2$—	H—	Ia	83	95	0.3	Liq.	1.4930	1.2801	50.48	50.43	$C_8H_{16}BrNO$	6.31	5.99	6.23
n-C_7H_{15}—	H—	Ia	81	110	0.25	*ca.* 20	1.4870	1.2357	55.30	54.93	$C_9H_{18}BrNO$	5.93	5.71	5.86
n-C_8H_{17}—	H—	Ia	80	119–120	0.25	*ca.* 26					$C_{10}H_{20}BrNO$	5.60	5.50	5.52
n-$C_{10}H_{21}$—	H—	Ia	79	130	0.2	38–40					$C_{12}H_{24}BrNO$	5.04	5.17	5.17

[a] All temperatures are uncorrected. [b] Some of these values were obtained on supercooled liquids. [c] von Braun, Jostes and Munch[2] reported m. p. 49°. [d] Miller and Johnson[3] reported b. p. 114–117° (9 mm.). [e] Bergmann, Dreyer and Radt[4] reported b. p. 85° (0.3–0.4 mm.) and noted compound was solid at room temperature but melted on warming in the hand. [f] Calcd.: Br, 44.39. Found: Br, 43.71, 44.10. [g] Calcd.: Br, 44.89. Found: Br, 44.10, 43.85. [h] Calcd.: Br, 41.18. Found: Br, 41.32, 41.33. [i] Micro-analyses by Arlington Laboratories, Fairfax, Virginia.

bromoacetyl bromide in 25 cc. of benzene was gradually added. The next day the crystals of amine salt were filtered out, the filtrate dried and distilled.

Method Ie.—This method differed from Method Ia only in that three equivalents of amine were used rather than two.

Method IIa.—For the preparation of bromoacetamides from amine hydrochlorides, an adaptation of the method of McKie[10] for chloroacetamides was used. In the reaction flask were placed 150 cc. of ethylene dichloride, 50 cc. of 40% *W/V* sodium hydroxide solution and 0.2 mole of the amine hydrochloride. After cooling to −10°, 0.2 mole of bromoacetyl bromide in 25 cc. of ethylene dichloride was added dropwise. The mixture was filtered, separated and the ethylene dichloride layer dried. The product was then distilled as in Method Ia.

Method IIb.—This method differed from the previous only in that 100 cc. of 20% *W/V* sodium hydroxide solution was used.

Method III.—The 500-cc. flask containing 150 cc. of chloroform, 0.4 mole of pyridine and 0.2 mole of amine hydrochloride was cooled to −5° and 0.2 mole of bromoacetyl bromide was added during half an hour, while keeping the temperature below 0°. The mixture was stirred half an hour longer. It was light-yellow and contained no solid. After washing with dilute hydrochloric acid and water, the solution was dried and distilled.

For the preparation of amides from aliphatic amines and bromoacetyl bromide Methods Ia and Ib are preferable, depending upon the water-solubility of the product. Fortunately, the amine salts of the lower amines are much less soluble in ethylene dichloride than those of the higher amines, making washing with water unnecessary, in Method Ib. When the amides are prepared from amine hydrochlorides Method IIa is preferable.

Summary

1. Twenty-three α-bromoacetamides have been prepared preliminary to evaluation of their fungicidal activity. Twenty of these are new compounds.

2. A general method for preparing amides from acid halides in ethylene dichloride is given.

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[10] McKie, *J. Chem. Soc.*, 2213 (1923).