mann and Lloyd V. Edgington in the preparation of the plant material, Rudolf Heitefuss for the malic acid determinations, Ernst Gaumann and Paul J. Allen for samples of lycomarasmin and fusaric acid.

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NEMATOCIDES

Screening Tests on Bromoacetates as Nematocides

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Many of the 53 bromoacetates synthesized and tested as nematocides against *Rhabditis* sp. and *Panagrellus* sp. were found to exhibit high activity. About two thirds of the esters gave an LD_{95} of less than 20 p.p.m., and about one half less than 10 p.p.m. Some were effective at the 1-p.p.m. level, most of these being esters of straight-chain alcohols having 6 to 12 carbon atoms. The effect of structural variations in the alcohol portion of the ester is discussed. Several of the compounds show sufficient promise to warrant further testing. The octyl, 4-bicyclohexylyl, heptyl, decyl, 4-sec-butylcyclohexyl, and hexyl esters gave an LD_{95} of less than 2 p.p.m.

SEVERAL ESTERS of bromoacetic acid were found to exhibit a marked lethal effect, in the course of screening a large group of miscellaneous organic compounds for toxicity to nematodes. To find out which of these compounds would be most effective, 53 bromoacetates were prepared and tested. The results indicated that the chemical structure of the alcohol moiety of the ester had an important effect on the nematocidal activity of the compound.

Preparation of Compounds

The bromoacetates were synthesized by azeotropic esterification of bromoacetic acid with the various alcohols. Benzene was used as a solvent and *p*-toluenesulfonic acid as a catalyst. The physical and chemical data of the esters prepared are presented in Table I. Only four of the esters have had their constants previously recorded in the literature—cyclohexyl (*3*), benzyl (*2*), 2-chloroethyl (*4*), and the diester of ethylene glycol (*1, 5*). The constants agree with those reported here.

Biological Tests

The compounds were screened against mixed populations of *Rhabditis* sp. and *Panagrellus* sp. according to the technique described by Taylor, Feldmesser, and Feder (*6*). In this procedure nematodes in small glass vials filled with sand were exposed to various dosages of each compound in a water-acetone solution or in a water emulsion. A dosage-response curve was plotted for each compound, as illustrated in Figure 1. The curves shown are typical of those obtained in this study. The phenethyl ester was selected because its response was practically a straight line and the 2-methylpentyl ester, because the actual straight-line response had to be approximated between several points. The dosages corresponding to LD_{50} and LD_{95} are the averages of three replicates and are given in Table I, which shows the compounds arranged in order of increasing LD_{95}.

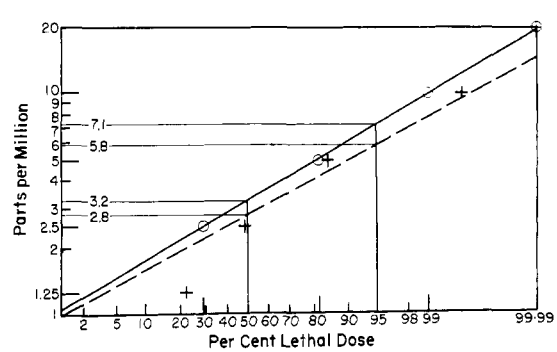

Figure 1. Typical dosage response curves

— Phenethyl bromoacetate
--- 2-Methylpentyl bromoacetate

Discussion

Several interesting facts are evident from the table. Approximately two thirds of the 53 compounds tested give an LD_{95} of less than 20 p.p.m. and about one half of less than 10 p.p.m. This is a high proportion of active compounds for such a series of related substances. There also seems to be a very wide difference between the LD_{95} and LD_{50} figures for many of the compounds, indicating that some of the dosage response curves are steep and others flat.

Among the seven most effective bromoacetates are five straight-chain aliphatic —hexyl, heptyl, octyl, decyl, and dodecyl. Some of the branched aliphatic esters, such as 1 = ethylpropyl, 2-ethylbutyl, 2-methylpentyl, 1-ethylpentyl, and 2-ethylhexyl also show considerable toxicity, but are not quite so effective as the straight chain compounds. A few of the substituted cyclohexyl esters, especially the para-substituted ones, are also toxic—namely, 4-bicyclohexylyl, 4-*sec*-butylcyclohexyl, and 4-isopropylcyclohexyl. The 2-isopropylcyclohexyl is much less effective than the corresponding para compound. The cyclohexyl ester itself is only slightly less active than the 4-methylcyclohexyl.

Table I. Toxicity to Nematodes of Bromoacetates and Their Chemical and Physical Data

Ester	Biological Data: LD_{95}, p.p.m.	Biological Data: LD_{50}, p.p.m.	Chemical Data: Empirical formula	Yield, %	Boiling Point: ° C.	Boiling Point: Mm. Hg	Refractive index, n_D^{25}
Octyl	0.8	0.3	$C_{10}H_{19}BrO_2$	90	137	13	1.4531
4-Bicyclohexylyl	1.07	0.3	$C_{14}H_{23}BrO_2$	94	140	0.8	1.5090
Heptyl	1.2	0.2	$C_9H_{17}BrO_2$	87	129–30	13	1.4532
Decyl	1.3	0.6	$C_{12}H_{23}BrO_2$	99	117–8	0.7	1.4565
4-*sec*-Butylcyclohexyl	1.6	1.1	$C_{12}H_{21}BrO_2$	71	163	13	1.4809
Hexyl	1.6	0.84	$C_8H_{15}BrO_2$	91	117–8	15	1.4568
Dodecyl	1.75	0.75	$C_{14}H_{27}BrO_2$	81	188–94	13	1.4574
4-Isopropylcyclohexyl	2.7	0.82	$C_{11}H_{19}BrO_2$	92	150	13	1.4802
p-Chlorophenethyl	2.75	1.75	$C_{10}H_{10}BrClO_2$	87	118	0.7	1.5460
p-Chlorobenzyl	3.75	2.25	$C_9H_8BrClO_2$	94	172	10	1.5542
Diester with 1,5-pentanediol	4.8	2.5	$C_9H_{14}Br_2O_4$	77	(46–7)[a]	..	..
Cyclohexyl	5.1	2.7	$C_8H_{13}BrO_2$	80	114	13	1.4852
[2-(*p*-Chlorophenoxy)-1-methyl]ethyl	5.3	3.3	$C_{11}H_{12}BrClO_3$	91	128–9	0.05	1.5370
4-Methylcyclohexyl	5.5	2.6	$C_9H_{15}BrO_2$	87	123	13	1.4783
2-Methylpentyl	5.8	2.8	$C_8H_{15}BrO_2$	96	104	13	1.4520
Cyclohexylethyl	5.9	3.0	$C_{10}H_{17}BrO_2$	92	145	13	1.4836
1-Ethylpropyl	6.3	2.65	$C_7H_{13}BrO_2$	86	86	13	1.4482
3-Phenylpropyl	6.7	2.8	$C_{11}H_{13}BrO_2$	99	174	13	1.5295
2-Ethylhexyl	6.8	2.9	$C_{10}H_{19}BrO_2$	93	129	13	1.4559
Phenethyl	7.1	3.2	$C_{10}H_{11}BrO_2$	85	155	12	1.5344
Cyclopentyl	7.45	3.5	$C_7H_{11}BrO_3$	75	101–2	10	1.4815
Citronellyl	7.8	2.8	$C_{12}H_{21}BrO_2$	76	93	0.1	1.4737
2-Ethylbutyl	7.8	4.0	$C_8H_{15}BrO_2$	87	105–6	12	1.4550
[2-(*o*-Chlorophenoxy)-1-methyl]ethyl	8.6	4.4	$C_{11}H_{12}BrClO_3$	89	127	0.05	1.5372
Benzyl	9.0	3.35	$C_9H_9BrO_2$	88	146	12	1.5412
(1-Methyl-2-phenoxy)ethyl	9.3	5.1	$C_{11}H_{13}BrO_3$	78	148	3.2	1.5276
1-Ethylpentyl	10.0	2.8	$C_8H_{17}BrO_2$	93	111	13	1.4508
1,3-Dimethylbutyl	12.5	6.2	$C_8H_{15}BrO_2$	85	92	13	1.4452
3-Chloropropyl	14.4	5.0	$C_5H_8BrClO_2$	63	127	12	1.4817
2-Chloroethyl	14.5	8.2	$C_4H_6BrClO_2$	70	101	13	1.4875
(2-Chloro-1-methyl)ethyl	15.0	4.0	$C_5H_8BrClO_2$	65	105–6	12	1.4770
2-Butoxyethyl	15.0	9.0	$C_8H_{15}BrO_3$	62	137–8	15	1.4548
p-Nitrobenzyl	18.0	4.0	$C_9H_8BrNO_4$	89	165	0.5	1.5698
Diester with 1,3-butanediol	18.5	10.0	$C_8H_{12}Br_2O_4$	83	140	1.2	1.4900
2-Phenoxyethyl	19.0	13.8	$C_{10}H_{11}BrO_3$	83	177	13	1.5387
2-Methoxyethyl	20.5	5.7	$C_5H_9BrO_3$	81	99	13	1.4609
Diester with ethylene glycol	21.0	13.0	$C_6H_8Br_2O_4$	56	173	13	1.5051
2-Isopropylcyclohexyl	22.0	2.4	$C_{11}H_{19}BrO_2$	72	140	13	1.4815
2-(2-Butoxyethoxy)ethyl	26.0	11.9	$C_{10}H_{19}BrO_4$	94	173–5	15	1.4582
(2-Methoxy-1-methyl)ethyl	28.0	12.6	$C_6H_{11}BrO_3$	75	99–100	13	1.4535
Tetrahydro-2-furfuryl	28.0	2.0	$C_7H_{11}BrO_3$	84	135	13	1.4848
2-(3-Phenoxypropoxy)propyl	30.0	13.8	$C_{14}H_{19}BrO_4$	92	140	0.2	1.5103
Tetrahydropyran-2-methyl	37.0	16.8	$C_8H_{13}BrO_3$	72	148–9	13	1.4867
2-(*p*-*tert*-Butylphenoxy)ethyl	43.0	16.2	$C_{14}H_{19}BrO_3$	89	150	0.8	1.5217
[2-(2,4-Dichlorophenoxy)-1-methyl]ethyl	47.0	2.5	$C_{11}H_{11}BrCl_2O_3$	91	139	0.1	1.5465
Tetradecyl	54.0	5.0	$C_{16}H_{31}BrO_2$	81	136–7	0.08	1.4600
2-(2-Methoxyethoxy)ethyl	60.0	24.9	$C_7H_{13}BrO_4$	73	146	13	1.4641
(1-Isobutyl-3-methyl)butyl	62.0	5.0	$C_{11}H_{21}BrO_2$	94	121	13	1.4480
2,2,2-Trichloroethyl	100.0	25.0	$C_4H_4BrCl_3O_2$	61	107	13	1.4968
[2-(*p*-*sec*-Butylphenoxy)-1-methyl]ethyl	130.0	3.1	$C_{15}H_{21}BrO_3$	90	133–6	0.08	1.5125
(4-Ethyl-1-methyl)octyl	169.0	72.0	$C_{13}H_{25}BrO_2$	95	160–1	13	1.4553
2-Butyloctyl	171.0	18.0	$C_{14}H_{27}BrO_2$	90	173	13	1.4588
Ester with 3,9-diethyl-6-tridecanol	175.0	150.0	$C_{19}H_{37}BrO_2$	96	145–6	0.1	1.4604

[a] Melting point.

The aralkyl and chlorine-substituted aralkyl esters are fairly active in the following order: *p*-chlorophenethyl, *p*-chlorobenzyl, 3-phenylpropyl, phenethyl, and benzyl. The chlorine substituted esters are more effective than the unsubstituted ones, the activity decreasing with the length of the alkyl chain. The substitution of a nitro group in the para position of the benzyl radical decreases its activity.

The esters containing an ether group which are most effective include [2-(*p*-chlorophenoxy)-1-methyl]ethyl, [2-(*o*-chlorophenoxy) - 1 - methyl]ethyl, (1-methyl-2-phenoxy)ethyl, 2-butoxyethyl, 2 - phenoxyethyl, and 2-methoxyethyl.

Most of these compounds contain the phenoxyethyl group and the activity seems to diminish with the decrease in molecular weight of the radical. Several other related esters did not show as much toxicity as the ones mentioned.

Three diesters were tested. Listed in order of activity they were 1,5 pentanediol, 1,3-butanediol, and the ethylene glycol diester. Here again the decrease in toxicity with decrease in molecular weight was evident.

Additional experiments are being conducted on and around nematode-infected plants to determine whether any of them will continue to be effective under practical conditions.

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