THE PRE-EMERGENT HERBICIDAL ACTIVITY OF CERTAIN ACETALDEHYDE AND CHLORO-SUBSTITUTED ALDEHYDE ADDITION PRODUCTS AND RELATED COMPOUNDS

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Three series of chloro-substituted aliphatic aldehyde addition products, mostly derived from chloral, together with related compounds, have been examined for pre-emergent herbicidal activity. The herbicidal investigations were carried out in the laboratory and greenhouse with both mono- and dicotyledonous plants as test species. Some of the compounds showed selective activity at low dosage rates per acre and appeared to warrant further examination under field conditions.

The chloral-nitro-paraffin and chloral-amide addition products showed selective herbicidal toxicity which might depend on their breakdown in soil to trichloroacetic acid. The unsaturated dehydration products of the nitro-alkanols, their acetyl derivatives and the corresponding methoxy compounds exhibited little toxicity towards any plant species tested. All active compounds tested were toxic towards wheat and other monocotyledonous species and almost inactive towards dicotyledonous plants.

Introduction

Among the simple chlorine-substituted aliphatic compounds, the α-chloroacetamides have been shown to possess selective herbicidal properties.[1-4]

Sodium trichloroacetate, dichloralurea (DCU) and 2,2-dichloropropionic acid (dalapon)[5] are also selective and are used commercially as herbicides.

In the present study certain chloro-substituted aldehyde addition products and related compounds have been examined for herbicidal properties both in laboratory and greenhouse tests.

Two other series of trichloroaldehyde reaction products, the chloral amides and chloral ureas, were also prepared and examined. All results have been statistically analysed and are discussed in relation to possible modes of action.

Experimental

Materials and methods

A. *Chemical preparations*

The compounds synthesised may be divided into three groups which will be considered separately.

(1) *Nitro-alcohols and related compounds*

These compounds, together with their physical properties and yields obtained, are listed in Table I.

(*a*) *Nitro-alcohols:* R·CH(OH)·CHR′·NO_2 (where R is CH_3, CH_2Cl, $CHCl_2$, CCl_3, and R′ is H, CH_3 or C_2H_5) were prepared by the method of Chattaway *et al.*[6, 7] or the slightly modified procedure of Eckstein & Urbanski[8] depending on an addition reaction between aldehyde and appropriate nitro-alkane in a faintly alkaline medium.

(*b*) *Acetoxy-nitro-alkanes:* R·CH(O·OC·CH_3)·CHR′·NO_2 (where R is CCl_3, and R′ is H, CH_3 or C_2H_5). These were prepared from the nitro-alcohols by the action of acetic anhydride,[6, 7] or, more satisfactorily, acetyl chloride, according to the method of Brower & Burkett.[9]

(*c*) *Nitro-alkenes:* R·CH:CR′·NO_2 (where R is CH_3 or CCl_3 and R′ is H, CH_3 or C_2H_5). These were prepared by deacetylation of the acetoxy-nitro-alkanes or by dehydration of the nitro-alcohols. The former method, described by Brower & Burkett,[9] employs anhydrous sodium carbonate in benzene. The chlorinated nitro-alcohols were dehydrated by the action of phosphorus pentachloride in chloroform.[9] 3-Nitrobut-2-ene was prepared by the action of phthalic anhydride on 3-nitrobutan-2-ol under reduced pressure.[10]

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(*d*) *Methoxy-nitro-alkanes:* $R{\cdot}CH(OCH_3){\cdot}CHR'{\cdot}NO_2$ (where R is CCl_3 and R′ is H, CH_3 or C_2H_5). These ethers were prepared by the action of sodium methoxide on the appropriate nitro-alkene.[11]

(2) *Addition compounds of chloral with urea and substituted ureas*

N-(2,2,2-Trichloro-1-hydroxyethyl)urea and bis-*N*-(2,2,2-trichloro-1-hydroxyethyl)urea were prepared by the method of Coppen & Titherley[12] involving the addition of chloral and urea under strictly defined conditions.

N′-(2,2,2-Trichloro-1-hydroxyethyl)-*NN*-dimethylurea was prepared by the reaction of chloral hydrate and *NN*-dimethylurea (cf. van der Zande[13]).

(3) *Addition compounds of chloral with amides*

The method used was similar to those of Feist,[14] Jacobsen[15] and Purgotti.[16] The compounds synthesised together with relevant data are given in Table I.

B. *Biological tests*

(1) *Greenhouse tests*

Box test.—Seeds of certain monocotyledonous crops and weeds and dicotyledonous crops were sown in wooden seed-boxes. The test compound was applied either by mixing the compound in the form of a dust with the soil prior to sowing,[17] or by spraying the soil surface with a solution in 50% aqueous acetone 48 h. after sowing. This test was used to give an initial rapid survey of toxicity and selectivity.

Pot test.—Small plastic pots of surface area 6·6 sq. in. and depth 2 in. were subsequently used to eliminate such factors as leaching and contamination. The relative toxicities of the compounds were obtained more precisely by this method. The compounds were applied with a pipette in aqueous acetone solution at known dosages 48 h. after planting the seeds and each pot was given 5 ml. of water daily. The vegetative growth was assessed 14 days after germination.[17]

Results of both box and pot tests are given in Table II.

Table I

Compounds prepared

No	Compound	Refractive index at temp. indicated	M.p. or b.p., ° c	Yield, %
1	1,1,1-Trichloro-3-nitropropan-2-ol		43–45	66
2	2-Acetoxy-1,1,1-trichloro-3-nitropropane		59–60	93
3	1,1,1-Trichloro-2-methoxy-3-nitropropane	1·4823[19]	88/2·2 mm.	34
4	1,1,1-Trichloro-3-nitroprop-2-ene	1·5162[20]	84/13 mm.	70
5	2-(1,1,1-Trichloro-3-nitropropyl) *N*-phenylcarbamate		125–128	35
6	1,1,1-Trichloro-3-nitrobutan-2-ol	1·5013[22]	84–86/0·4 mm.	61
7	2-Acetoxy-1,1,1-trichloro-3-nitrobutane	1·4810[18]	90/0·4 mm.	90
8	1,1,1-Trichloro-2-methoxy-3-nitrobutane	1·4833[18]	120–121/16 mm.	37
9	1,1,1-Trichloro-3-nitrobut-2-ene	1·5152[19]	95–97/14 mm.	80
10	1,1,1-Trichloro-3-nitropentan-2-ol	1·4956[22]	99–100/1 mm.	30
11	2-Acetoxy-1,1,1-trichloro-3-nitropentane	1·4778[17]	108/1·5 mm.	74
12	1,1,1-Trichloro-2-methoxy-3-nitropentane	1·4892[18]	100–103/2 mm.	20
13	1,1,1-Trichloro-3-nitropent-2-ene	1·5105[15]	68–69/1 mm.	71
14	3-Nitropropan-2-ol	1·4402[21]	62–66/1·5 mm.	49
15	3-Nitrobutan-2-ol	1·4412[22]	64/1 mm.	47
16	3-Nitrobut-2-ene	1·4630[17·6]	59–62/17 mm.	61
17	1-Chloro-3-nitropropan-2-ol		85/0·6 mm.	45
18	1-Chloro-3-nitrobutan-2-ol		85–86/1·7 mm.	54
19	1,1-Dichloro-3-nitropropan-2-ol		102/1·0 mm.	42
20	1,1-Dichloro-3-nitrobutan-2-ol		84–85/0·4 mm.	42
21	Trichloroacetic acid (TCA)		58	
22	Trichloroacetaldehyde		96/760	
23	Chloral hydrate		52	
24	*N*-(2,2,2-trichloro-1-hydroxyethyl)urea		151–153	72
25	Bis-*N*-(2,2,2-trichloro-1-hydroxyethyl)urea		194–196	66
26	*N*′-(2,2,2-Trichloro-1-hydroxyethyl)-*NN*-dimethylurea		156	27
27	*N*-(2,2,2-Trichloro-1-hydroxyethyl)acetamide		157–158	66
28	*N*-(2,2,2-Trichloro-1-hydroxyethyl)propionamide		161–162	68
29	*N*-(2,2,2-Trichloro-1-hydroxyethyl)isobutyramide		146·5–148	84
30	*N*-(2,2,2-Trichloro-1-hydroxyethyl)trimethylacetamide		157–158	71
31	*N*-(2,2,2-Trichloro-1-hydroxyethyl)chloroacetamide		141–142	76
32	*N*-(2,2,2-Trichloro-1-hydroxyethyl)phenylacetamide		144	84
33	*N*-(2,2,2-Trichloro-1-hydroxyethyl)-*p*-chlorophenylacetamide		167–168	72
34	Trichloroacetamide		140·5–141	42

Table II

Effect of compounds on growth in greenhouse tests

Compound	Dosage medium	Dosage, lb./acre	Activity in box test*							Activity in pot test†	
			Ryegrass	Wheat	Maize	Wild oats	Mustard	Cabbage	Sugar beet	Wheat	Cabbage
Control	—	—	4	4	4	4	4	4	4	8	8
1	Dust	50	3	1	—	—	—	4	—	—	—
1	Spray	50	—	3	2	4	4	4	4	—	—
2	Dust	50	4	4	—	—	—	4	—	—	—
5	Dust	50	4	4	—	—	—	4	—	—	—
6	Spray	50	—	3	2	3	4	4	4	—	—
6	Dust	50	2	1	—	—	—	4	—	—	—
6	Solution	30	—	—	—	—	—	—	—	1	8
7	Dust	50	4	3	—	—	—	4	—	—	—
10	Spray	50	—	4	3	4	4	4	4	—	—
10	Solution	30	—	—	—	—	—	—	—	6	3
14	Spray	40	—	4	4	4	4	4	4	—	—
15	Spray	40	—	4	4	4	4	4	4	—	—
17	Dust	30	4	4	—	—	—	4	—	—	—
18	Dust	20	4	4	—	—	—	4	—	—	—
19	Dust	30	4	4	—	—	—	4	—	—	—
20	Dust	50	4	4	—	—	—	4	—	—	—
22	Solution	10	—	—	—	—	—	—	—	1	8
23	Solution	10	—	—	—	—	—	—	—	1	8
24	Dust	30	1	1	—	—	—	4	—	—	—
24	Solution	10	—	—	—	—	—	—	—	1	8
24	Solution	3	—	—	—	—	—	—	—	4	8
25	Dust	50	2	2	—	—	—	3	—	—	—
25	Solution	10	—	—	—	—	—	—	—	4	2
26	Solution	10	—	—	—	—	—	—	—	2	8
26	Solution	3	—	—	—	—	—	—	—	5	8
27	Dust	10	1	1	—	—	—	—	—	—	—
27	Solution	10	—	—	—	—	—	4	—	6	8
28	Solution	10	—	—	—	—	—	—	—	4	8
29	Solution	30	—	—	—	—	—	—	—	6	7
30	Solution	30	—	—	—	—	—	—	—	8	6
31	Solution	10	—	—	—	—	—	—	—	3	4
32	Solution	30	—	—	—	—	—	—	—	4	7
33	Solution	30	—	—	—	—	—	—	—	8	8
34	Solution	10	—	—	—	—	—	—	—	2	6

* Figures given express vegetative growth :

4 under 25% plants affected
3 25 to 75% affected
2 over 75% affected
1 all plants dead—not tested

Results were taken 25 days after spraying and 15 days after germination when dust used.

† Figures express vegetative growth on a scale from 0 (death and no germination) to 8 (growth as control)

(2) *Statistical analysis of comparative toxicity*

The herbicidal activity of compounds 1–13, excluding Compound 5, were compared with that of trichloroacetic acid (Compound 21) using the plastic pots, assessment being made of the growth of the wheat seedlings after 28 days. These were measured from soil level to the tip of the longest leaf; percentage germination was also noted.

The compounds were tested in three batches, trichloroacetic acid being included in each test and the relative activities of the compounds in each batch, as indicated by the average growth in each pot, were subjected to statistical analysis.

Ten wheat seeds were planted in each pot and watered immediately and thereafter 5 ml. of water were applied to each pot every day for the duration of the experiment. Each compound was tested at three concentrations, 0·01M, 0·03M and 0·09M and six pots were used for each concentration. Treatment consisted of applying 2 ml. of a 50% aqueous acetone solution of the compound evenly from a pipette to the soil surface 48 h. after planting the seeds. The concentrations 0·01–0·09M were chosen to correspond roughly with the dosage rates 10–50 lb./acre used in the preliminary experiments. The 90 treated and 6 control pots were then randomised on a greenhouse bench.

The figures for aerial growth and germination percentages are shown in Table III.

(3) *The persistence of 1,1,1-trichloro-3-nitropropan-2-ol in the soil*

Wheat seeds were planted in 24 out of 120 plastic pots filled with John Innes Compost No. 2, 10 seeds being placed in each pot. All the pots were watered initially and approximately 5 ml. of water were applied to each pot every day for the duration of the experiment. Forty-eight h. after the pots had been filled a 0·09M solution of 1,1,1-trichloro-3-nitropropan-2-ol in 50% aqueous acetone was applied evenly over the surface of the compost in half of the pots (2 ml. per pot) including half of those already sown with wheat. Twelve chemically treated and 12 untreated pots were then taken and 10 wheat seeds planted in each. Further batches of 24 pots were sown with wheat seeds after 2, 7 and 14 days.

Three weeks after the chemical had been applied to the pots the growth of the wheat seedlings in all pots was estimated by measuring the height of the seedling from soil level to the tip of the longest leaf. Observations were also made on the percentage of seeds germinated. Results giving both the average growth per treatment as a percentage of the control growth and the percentage germination are presented in Table IV.

Table III

Effect of chloral nitro-alcohols and related compounds on germination and the aerial growth of wheat seedlings after 28 days

Group	Compound no.	0·01M		0·03M		0·09M	
		Growth, cm.	% Germination	Growth, cm.	% Germination	Growth, cm.	% Germination
1	Control	203·4	88·3				
	6	43·02***	78·4	22·70***	61·7	7·10***	5·0
	7	185·00	71·7	79·53***	60·0	16·83***	15·0
	8	216·70	78·4	186·17	58·3	65·16***	16·7
	9	217·98	63·3	210·95	58·3	19·90***	8·3
	21	12·36***	90·0	0***	80·0	0***	61·7
2	Control	196·90	63·4				
	6	112·28**	80·0	35·26***	61·6	16·45***	10·0
	10	154·56	65·0	44·93***	43·3	0***	0
	11	198·30	76·7	102·75***	46·7	43·30***	10·0
	13	208·72	60·0	224·83	31·7	115·55**	11·7
	16	192·71	73·4	202·04	63·4	29·05***	6·7
	21	7·93***	73·4	0***	61·6	0***	66·7
3	Control	202·43	80·0				
	1	124·17***	70·0	31·92***	68·3	0***	3·3
	2	209·13	86·7	90·04***	53·3	31·90***	8·3
	3	212·25	85·0	208·91	71·7	114·29**	63·4
	4	213·81	66·7	209·92	66·7	80·25***	8·3
	12	205·50	81·7	187·52	71·7	38·67***	16·7
	21†	50·77***	76·7	12·85***	78·4	0***	66·7

Figures given for each concentration are the sums of the average in cm. from six pots. Results significantly different from the control: *at 5% level, **at 1% level, ***at 0·1% level.

† Compound 21 in this batch was tested at 0·0012M, 0·006M and 0·03M. At concentrations higher than 0·0012M the first leaf did not emerge from the coleoptile.

Table IV

The persistence of 1,1,1-trichloro-3-nitropropan-2-ol in the soil

No. of days seeds were sown after application of chemical	No. of days results were taken after sowing seeds	Growth as % of control	% germination	
			Untreated seeds	Treated seeds
−2	23	12·3	55·0	11·7
0	24	9·3	48·3	1·7
2	19	9·0	34·2	16·7
7	14	18·7	29·2	21·7
12	7	31·2	38·3	20·8

(4) *Wheat Petri-dish test*

Certain of the compounds were tested for root-inhibiting action by the wheat Petri-dish assay,[17] which involves the application of an aqueous solution of the compound at a known concentration to previously germinated wheat seeds on filter paper in an 11-cm. Petri-dish. After 36 h. in a humidity box in a constant-temperature room at 27° the tap-root lengths were determined and compared with the average length of the roots from the control seeds. The results (Table V) showed that in the case of the compounds tested neither root nor shoot growth was inhibited during that period. The effect of incubating chloral-acetamide (Compound 27) with soil before application to the growing seedlings was then assessed and again no inhibition was found.

The compounds were then applied to dormant seeds grown on either filter paper or soil, and here, both root and shoot inhibition was found (Table VI). A similar effect was noted

when trichloroacetic acid, a possible toxic metabolite, was applied to growing seeds and then to dormant seeds planted on filter paper. It may be seen from Table VI that the amount of inhibition was greater when soil was present. Observations taken from greenhouse experiments show that when the compounds are applied to seeds growing in soil the shoots are inhibited but there is only slight root inhibition.

Table V

Effect of certain compounds in the normal wheat Petri-dish test

Compound no.	1 p.p.m.		10 p.p.m.		100 p.p.m.	
	Root	Shoot	Root	Shoot	Root	Shoot
Control	6·0	3·8	6·3	3·7	6·0	3·7
26	6·3	3·7	6·2	3·6	5·7	3·6
27	6·3	3·7	6·0	3·8	6·3	3·6
33	6·3	3·7	5·4	3·7	5·9	3·5

Figures given are average measurements of 15 seeds in cm.

Table VI

Effect of Compound 27 (500 p.p.m.) on dormant seeds planted on filter paper or soil

	Plate 1		Plate 2		Plate 3		Root average, cm.	Ratio
	Root	Shoot	Root	Shoot	Root	Shoot		
Filter paper								
Control	7·2	4·3	7·1	4·3	6·8	4·0	7·0	
Test	5·8	3·3	5·6	3·4	5·6	3·2	5·6	0·80
Soil								
Control	7·2	4·9	5·2	4·6	6·7	4·5	6·4	
Test	3·8	2·7	3·9	2·7	3·6	2·7	3·8	0·59

Figures given are average measurements of 15 seeds in cm.

$$\text{The ratio} = \frac{\text{average root length of wheat seeds in test solution}}{\text{average root length of control wheat seeds}}$$

Discussion

In the following discussion, to facilitate references to Tables, the name of each compound is followed by its number in brackets.

From the results of the tests in seed boxes and pots, it is seen that, while apparently a CCl_3 group is necessary for selective phytotoxicity (compare compounds 14, 15 and 17–20 which are ineffective with compounds 1 and 6), all compounds having this group are not phytotoxic (see the trichlorinated α-nitroalkenes and α-nitro-ethers; cf. also DDT).

It is postulated that the phytotoxic effect of the active trichloromethyl-substituted compounds is due to their breakdown to trichloroacetic acid. This is based on the observations that (i) the selectivity of all the herbicidal compounds and (ii) the morphological abnormalities produced in monocotyledonous plants strongly resemble the effects of low concentrations of trichloroacetic acid. The seedlings were stunted, with twisted leaves and showed a tendency to tiller. When wheat seeds were planted in soil 7–14 days after treatment with 1,1,1-trichloro-3-nitropropan-2-ol (1), germination relative to control (Table IV) was only slightly affected as with trichloroacetic acid (21) at concentrations 0·01–0·09M (Table III); furthermore, the seedlings markedly resembled those obtained when trichloroacetic acid was applied to the soil shortly after planting. It is of interest that the addition products of chloral with urea, amides and nitro-alkanes should show a similar biological action when applied at comparable strengths. Chloral-chloroacetamide (31) is a particularly interesting compound, in that is shows the biological activity of both probable degradation products, exhibiting the characteristic effects of trichloroacetic acid on wheat and the high activity of chloroacetamide towards cabbage.[17] Evidence presented in Tables IV–VI indicates that breakdown of the active compounds to trichloroacetic acid probably takes place in the soil, a process which appears more difficult with the larger molecules.

Some consideration has been given to the mechanism of this degradation. One possibility

is that the nitro-alcohols $CCl_3{\cdot}CH(OH){\cdot}CRR'{\cdot}NO_2$ are dehydrated to an alkene $CCl_3{\cdot}CH{:}CR{\cdot}NO_2$ which is then oxidised to $CCl_3{\cdot}CO_2H$. The acetylated nitro-alcohols would be first hydrolysed to the alcohol which is transformed to the alkene or might lose acetic acid to give the alkene direct, whereas the methyl ethers would be expected to be much more stable. This is borne out by the results in Table III which show that the alcohols are most effective in inhibiting growth, the acetyl derivatives are less active, whilst the methoxy and unsaturated compounds are almost inactive except at the highest concentration used. In addition, the latter two classes of compounds, although effective at high concentrations in preventing germination of wheat, produced almost no abnormal growth effects in the seedlings. It seems probable, therefore, that the action of the hydroxy and acetoxy compounds differs not only in degree but also in type from that of the methoxy and unsaturated derivatives and that a free hydroxyl group is necessary for maximum selective action. These results suggest that the breakdown of the nitro-alcohols to trichloroacetic acid does not involve a dehydration to the alkene and that the acetyl derivatives are hydrolysed to the free alcohol prior to further breakdown.

It would appear therefore that disproportionation of the molecule probably takes place to give the original reactants. This is supported by the known reversibility of this type of condensation and the inactivity of the ethers which could not undergo such a disproportionation.

The fact that all four classes of nitro-compounds were more effective in reducing germination than trichloroacetic acid (Table III) may be due to their higher lipoid solubility. The unsaturated derivatives are the most lipophilic of these compounds and these, in general, were the most effective in reducing germination at the lowest concentration used. Since a non-chlorinated analogue, however, 3-nitrobut-2-ene (16), was also effective in inhibiting germination it may well be that breakdown to trichloroacetic acid is unnecessary for this type of biological action.

From the results presented in this paper it would appear that the active compounds studied are toxic to monocotyledonous species by virtue of their degradation to trichloroacetic acid, and thus differ in their activity from both the urea and amide series of herbicides with which they have recently been associated.[18] It is suggested that certain of these compounds notably chloral-acetamide (27), monochloral-urea (24) and 1,1,1-trichloro-3-nitrobutan-2-ol (6) warrant further investigation under field conditions.

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