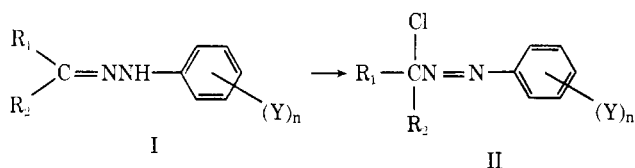# Herbicidal Activity of Phenylhydrazones and Related Azo Compounds

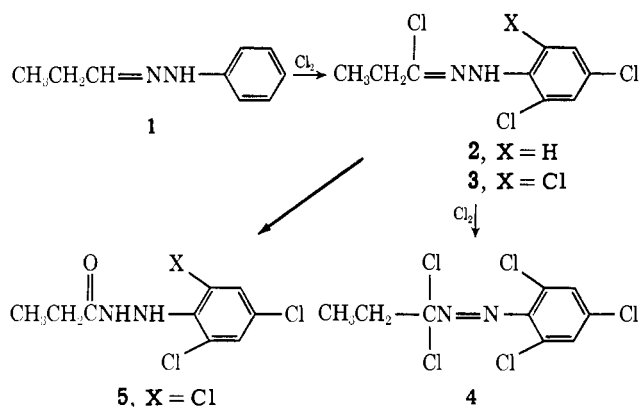Malcolm W. Moon,* Alan R. Friedman, and Arnolds Steinhards[1]

Propionyl chloride (2,4-dichlorophenyl)hydrazone, propionyl chloride (2,4,6-trichlorophenyl)hydrazone, and 1',1',2,4,6-pentachlorobenzeneazopropane were prepared by the reaction of propionaldehyde phenylhydrazone with chlorine. The three chlorination products were active as postemergence contact herbicides at rates as low as 1 lb per acre. The herbicidal activity of these and related phenylhydrazones and azo compounds is described.

Recent investigations in our laboratories have afforded a variety of biologically active phenylhydrazones (I). Several series of acid chloride phenylhydrazones

(I, R_1 = Cl) have shown high miticidal activity (Kaugars and Gemrich, 1969; Moon et al., 1972) and one compound, benzoyl chloride (2,4,6-trichlorophenyl)hydrazone, is presently being developed as an acaricide under the proposed trademark Banamite. We have also found that many phenylhydrazones react with chlorine to give α-chlorinated azo compounds (II) (Moon, 1972a,b,c). For example, propionaldehyde phenylhydrazone (1) reacts with 3 and 4 equiv of chlorine to

give propionyl chloride (2,4-dichlorophenyl)hydrazone (2) and propionyl chloride (2,4,6-trichlorophenyl)hydrazone (3), respectively, and with excess chlorine to give 1',1',2,4,6-pentachlorobenzeneazopropane (4). Compounds 2, 3, and 4 are highly active as postemergence herbicides. The herbicidal activity of these and related phenylhydrazones and azo compounds is described.

CHEMICAL METHODS

The acid chloride phenylhydrazones and azo compounds described herein are liquids or low melting solids. Structures and purities were determined by nmr, tlc, gc, ir, and mass spectral analyses; satisfactory elemental analyses (±0.3%) were obtained for all compounds.

The (2,4,6-trichlorophenyl)hydrazones 6–12 (Table I) were prepared by literature methods (Chattaway and Irving, 1931; Grammaticakis, 1967; Humphries et al., 1925; Moon, 1972a,c) and were chlorinated to afford the corresponding azo compounds 4, 14, and 16–19 (Table I) (Moon, 1972a,c). Reaction of propionaldehyde phenylhydrazone (1) with 3 equiv of chlorine in carbon tetrachloride followed by rapid chromatography of the product on silica gel gave, as the first product eluted from the column, propionyl chloride (2,4-dichlorophenyl)hydrazone (2). Propionyl chloride (2,4,6-trichlorophenyl)hydrazone (3) was prepared by reaction of propionaldehyde (2,4,6-trichlorophenyl)hydrazone (6) with 1 equiv of chlorine in carbon tetrachloride; compounds 40–42 (Table V) were prepared by the same method.

The synthesis of 1',1',2,4,6-pentachlorobenzeneazopropane (4) by chlorination of propionaldehyde phenylhydrazone has been described (Moon, 1972a). Compounds 20–24 (Table III) were prepared similarly by chlorination of the appropriate aldehyde phenylhydrazone and were purified by silica gel chromatography. Chlorination of isobutyraldehyde m-tolylhydrazone, isobutyraldehyde (3-chlorophenyl)hydrazone, and isobutyraldehyde (2,3,4,5,6-pentafluorophenyl)hydrazone gave 25, 26, and 27, respectively (Table III). Compound 28 was prepared by the reaction of 41 with trifluoromethyl hypofluorite in chlorotrifluoromethane at −60°. Reaction of 41 with potassium cyanide in methanol gave 47, and this was further reacted with chlorine to give 29.

Chlorination of ethyl chloroglyoxylate 2-[(2,4,6-trichlorophenyl)hydrazone] (Chattaway and Daldy, 1928) gave ethyl dichloro[(2,4,6-trichlorophenyl)azo]acetate (30) (Moon, 1972b); compounds 31–36 (Table IV) were prepared similarly. Reaction of ethyl pyruvate 2-[(2,4,6-trichlorophenyl)hydrazone] with chlorine or tert-butyl hypochlorite gave ethyl 2-chloro-2-[(2,4,6-trichlorophenyl)azo]propionate (38) (Moon, 1972b). Compound 39 was prepared in the same manner from ethyl 2-oxobutyrate 2-[(2,4,6-trichlorophenyl)hydrazone].

Propionic acid (2,4,6-trichlorophenyl)hydrazide (5), mp 120–124°, was prepared by reaction of (2,4,6-trichlorophenyl)hydrazine with propionyl chloride in pyridine. Reaction of pivalic acid phenylhydrazide with phosphorus pentachloride in carbon tetrachloride by the procedure of Pechmann and Seeberger (1894), followed by decomposition of the initially formed adduct with phenol gave pivaloyl chloride phenylhydrazone (44); the pivaloyl chloride phenylhydrazones 43–46 (Table V) were prepared by the same procedure.

BIOLOGICAL METHODS

Herbicide testing data were obtained in the greenhouse using a soil composed of equal parts by volume of topsoil, peat moss, and sand. Initial testing involved a single treatment in which

Table I. Postemergence Herbicidal Activities of Various (2,4,6-Trichlorophenyl)hydrazones and Related Azo Compounds

R₁	R₂	Compound no.	Herbicidal activity, 10 lb/acre	X	Compound no.	Herbicidal activity, 10 lb/acre
C₂H₅	H	6ᵃ	0			
C₂H₅	Cl	3	10	Cl	4ᵃ	10
CH₃	CH₃	7ᵇ	0	H	13ᵃ	0
CH₃	CH₃			Cl	14ᵃ	0
CH₃	CH₃			CN	15ᵃ	0
C₆H₅	H	8ᵇ	0			
C₆H₅	Cl	9ᶜ	0	Cl	16ᵃ	10
C₆H₅	CH₃	10ᵈ	0	Cl	17ᵃ	0
C₆H₅	C₆H₅	11ᵇ	0	Cl	18ᵃ	0
Cl	Cl	12ᵉ	0	Cl	19ᵉ	1.4

ᵃ Moon (1972a).   ᵇ Chattaway and Irving (1931).   ᶜ Humphries *et al.* (1925).   ᵈ Grammaticakis (1967).   ᵉ Moon (1972c).

the seven weed species were sown in rows across a 5 in. × 7 in. tray. All other testing involved two replications with four weed species being planted in the corners of a 5 in. × 5 in. tray.

The chemicals were formulated as 50% emulsifiable concentrates by the addition of an equal weight of a solution of toluene containing 10% Tween 20; application rates are calculated on the basis of the active ingredient. For initial testing the formulated chemical was dispersed in water and applied at 10 lb per acre to the following weed species: field bindweed (*Convolvulus arvensis*), buckhorn plantain (*Plantago lanceolata*) large crabgrass (*Digitaria sanguinalis*), curly dock (*Rumex crispus*), johnsongrass (*Sorghum halepense*), wild oat (*Avena fatua*), and yellow foxtail (*Setaria glauca*). The plants were sprayed 14 days after seeding and the treatments were evaluated 21 days after spraying using a 0 (no effect) to 10 (plants dead) scale relative to an untreated check; the data in the tables are averaged for the seven weed species.

Active chemicals were then applied at rates of 6, 3, and 1 lb per acre to the following broadleaved weeds: curly dock (*Rumex crispus*), jimsonweed (*Datura stramonium*), milkweed (*Asclepias syriaca*), black nightshade (*Solanum nigrum*), redroot pigweed (*Amaranthus retroflexus*), purslane (*Portulaca oleracea*), velvetleaf (*Abutilon theophrasti*), and yellow rocket (*Barbarea vulgaris*). The plants were treated 21 days after seeding and had two true leaves; the treatments were evaluated 25 days after application and results were averaged as for the initial testing. In this test the herbicide standard dinoseb gave an average reading of 5.6, 4.4, and 2.8 at 2, 1, and 0.5 lb per acre, respectively; dinoseb did not control velvetleaf, pigweed, and purslane at these rates.

Compound 4 was further evaluated on additional species at rates of 2 and 1 lb per acre, with the data being recorded as the percent control of above-ground plant weight relative to untreated checks (Table II).

RESULTS AND DISCUSSION

A series of eight (2,4,6-trichlorophenyl)hydrazones (3, 6–12) was prepared with the substituents R₁ and R₂ (Structure I) chosen from hydrogen, alkyl, phenyl, and chlorine, and these were chlorinated to give the corresponding azo compounds 4, 14, and 16–19. The only phenylhydrazone active as a herbicide was propionyl chloride (2,4,6-trichlorophenyl)hydrazone (3) (Table I). Activity in the azo series was limited to 1′,1′,-

2,4,6-pentachlorobenzeneazopropane (4) and 1′,1′,2,4,6-pentachloro-1′-phenylbenzeneazomethane (16), products formed by chlorination of aldehyde phenylhydrazones (Table I).

Compound 4 showed postemergence herbicidal activity on many weed species at rates as low as 1 lb per acre (Table II). It was a contact herbicide, more active on broadleaved species than on grasses. At rates near 10 lb per acre, 4 also had preemergence activity. Compound 4 was one of a series of herbicidally active 1′,1′-dichlorobenzeneazoalkanes (Table III). Activity was retained when the size of the alkyl group R₁ was varied (20–24) or when additional substituents were placed in the benzene ring (25–27); the (pentafluorophenyl)hydrazone 27 was considerably less active than the other compounds, however. Replacement of an α-chlorine substituent (X) by fluorine (28) or cyanide (29) gave compounds with reduced herbicidal activity. Further, while for optimum activity the substituent R₁ must be alkyl, activity was also found when R₁ was phenyl (16) or carboethoxy (30).

Although ethyl dichloro[(2,4,6-trichlorophenyl)azo]acetate (30) was less active than 4, activity of the azo esters was investigated further (Table IV). The methyl (31), isopropyl (32), and n-butyl (33) ester homologs were less active than 30 and variation of the substitution pattern in the benzene ring (34–36) gave no activity improvement. Chemicals with better activity were obtained when one of the α-chlorine substituents (X) was replaced with an alkyl group (37–39).

The activity of propionyl chloride (2,4,6-trichlorophenyl)-hydrazone (3) and related phenylhydrazone herbicides is shown in Table V. The active chemicals were contact herbicides whose broad spectrum postemergence activity was very similar to that found for the azo compounds of Table III; the phenylhydrazones were not active as preemergence herbicides at 10 lb per acre. The most active chemicals were the (2,4-dichlorophenyl)hydrazone 2 and (2,4,6-trichlorophenyl)-hydrazones 3 and 40–42. Activity was found for other benzene ring substitution patterns (43, 44), but the nitrophenyl-hydrazones 45 and 46 were not active as herbicides. Variation in the size of the alkyl residue (3, 40–42) had little effect on activity, while replacement of the acid chloride function with a cyano group (47) eliminated activity.

The mode of action of these new phenylhydrazone herbicides has not been studied to date; they may act, as do other series of biologically active phenylhydrazones (Büchel and

Table II. Percent Control[a] of Various Species by Postemergence Application
of 1′,1′,2,4,6-Pentachlorobenzeneazopropane[b] (4)

Species	Herbicidal activity		Species	Herbicidal activity	
	2 lb/acre	1 lb/acre		2 lb/acre	1 lb/acre
Chickweed (Stellaria media)	99	90	Bahia grass (Paspalum notatum)	86	72
Black nightshade (Solanum nigrum)	98	95	Barnyard grass (Echinochloa crusgalli)	96	62
Coffeeweed (Daubentonia texana)	70	70	Black grass (Alopecurus myosuroides)	71	60
Dandelion (Taraxacum officinale)	96	92	Bluegrass, Merian (Poa pratensis)	100	60
Curly dock (Rumex crispus)	96	77	Crabgrass (Digitaria sanguinalis)	95	79
Milkweed (Asclepias syriaca)	90	85	Downy brome (Bromus tectorum)	54	47
Morning glory (Ipomoea purpurea)	81	78	Green foxtail (Setaria viridis)	96	71
Pale smartweed (Polygonum lapathifolium)	99	90	Johnsongrass (Sorghum halepense)	72	58
Pepperweed (Lepidium campestre)	92	66	Quack grass (Agropyron repens)	75	59
Shepherd's purse (Capsella bursa-pastoris)	100	96	Red millet (Setaria italica)	88	85
Sesbania (Sesbania exaltata)	100	84	Ripgut brome (Bromus rigidus)	67	56
Star thistle (Centaurea solstitialis)	98	91	Rice (Oryza sativa)	34	34
Velvetleaf (Abutilon theophrasti)	84	84	Rye, perennial (Lolium perenne)	80	49
White cockle (Lychnis alba)	100	75	Wild oat (Avena fatua)	91	57
Wild mustard (Brassica kaber)	96	87	Average control: broadleaves	94	85
Yellow rocket (Barbarea vulgaris)	100	98	Average control: grasses	79	60

[a] The figures represent the percent control of above-ground plant growth relative to an untreated check. [b] The chemical formulation used contained (by weight) 4 (50%), xylene (45%), Agrimul A-300 (2.5%), and Agrimul N-300 (2.5%).

Table III. Postemergence Herbicidal Activity of Benzeneazoalkanes

$$R_1 - \overset{\overset{\displaystyle X}{|}}{\underset{\underset{\displaystyle Cl}{|}}{C}} N = N - \langle\text{phenyl}\rangle (Y)_n$$
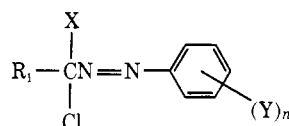
Compound no.	R₁	X	(Y)ₙ	Herbicidal activity		
				10 lb/acre	3 lb/acre	1 lb/acre
20	CH₃–	Cl	2,4,6-Cl₃	9.7[a]	9.8	6.4
4[b]	CH₃CH₂–	Cl	2,4,6-Cl₃	10[c]	10	7.8
21	CH₃CH₂CH₂–	Cl	2,4,6-Cl₃	7.0	9.4	7.4
22	(CH₃)₂CH–	Cl	2,4,6-Cl₃	9.3	10	8.8
23	(CH₃)₃C–	Cl	2,4,6-Cl₃	7.0	10	8.9
24	n-C₅H₁₁–	Cl	2,4,6-Cl₃	9.8[c]	9.9	8.1
16[b]	C₆H₅–	Cl	2,4,6-Cl₃	10	3.1[d]	
25	(CH₃)₂CH–	Cl	2,4,6-Cl₃-3-CH₃	9.9[c]	10	9.4
26	(CH₃)₂CH–	Cl	2,3,4,6-Cl₄	9.5	8.8	6.1
27	(CH₃)₂CH–	Cl	2,3,4,5,6-F₅	4.7	1.9	0
28	(CH₃)₂CH–	F	2,4,6-Cl₃	4.5	0	0
29[e]	(CH₃)₂CH–	CN	2,4,6-Cl₃	0		
30[f]	CH₃CH₂OC(=O)–	Cl	2,4,6-Cl₃	10		

[a] Average preemergence control on the same species at 10 lb per acre was 4.7. Moon (1972a). [c] Average preemergence control at 10 lb per acre was between 7.3 and 9.0. [d] At 6 lb per acre 16 gave an average reading of 6.1 on broadleaves. [e] Mp 60–62°. [f] Moon (1972b).

Draber, 1971; Heytler, 1963; Parker and Summers, 1970), by uncoupling oxidative phosphorylation. As 3 is a reactive chemical, reaction with nucleophiles may be involved in the toxic process. This could, for example, involve hydrolysis of 3 to propionic acid (2,4,6-trichlorophenyl)hydrazide (5). However, while hydrazides closely related to 5 are known to affect oxidative phosphorylation (Pagani et al., 1967; Sumina, 1967), 5 showed little herbicidal activity when applied to intact plants.

The azo compounds may be herbicidally active per se or alternately may be reduced in vivo to an active phenylhydrazone. Reductions of substituted azobenzenes at the azo linkage in mammalian and insect systems have been reported (Hernandez et al., 1967; Mueller and Miller, 1949; Shargel et al., 1972; Trefouel et al., 1935). In preliminary experiments we have found that homogenates of bean leaves convert 30 to ethyl chloroglyoxylate 2-[(2,4,6-trichlorophenyl)-hydrazone] (48) and 38 to ethyl pyruvate 2-[(2,4,6-trichloro-

Table IV. Postemergence Herbicidal Activity of Azo Esters

$$RO-\overset{\overset{O}{\|}}{C}\underset{\underset{X}{|}}{\overset{\overset{Cl}{|}}{C}}-N=N-\under{}(Y)_n$$

Com-pound no.	RO	X	$(Y)_n$	Herbicidal activity		
				10 lb/acre	6 lb/acre	3 lb/acre
31[a]	CH₃O–	Cl	2,4,6-Cl₃	6.2	4.8	
30[a]	C₂H₅O–	Cl	2,4,6-Cl₃	7.9	6.2	4.6
32	(CH₃)₂CHO–	Cl	2,4,6-Cl₃	10	2.6	0.8
33	CH₃CH₂CH₂CH₂O–	Cl	2,4,6-Cl₃	4.0	3.2	1.6
34	CH₃CH₂O–	Cl	2,4-Cl₂	9.6	3.1	1.0
35[a]	CH₃O–	Cl	2,6-Cl₂-4-CH₃	4.5	4.6	0.9
36[a]	CH₃O–	Cl	2,4,6-Cl₃-4-CH₃	2.9	3.4	0.9
37	CH₃O–	CH₃	2,4,6-Cl₃	5.7	7.8	5.8
38[a]	CH₃CH₂O–	CH₃	2,4,6-Cl₃	7.0	8.3	6.4
39	CH₃CH₂O–	CH₃CH₂	2,4,6-Cl₃	5.5	7.8	5.8

[a] Moon (1972b).

Table V. Postemergence Activity of Acid Chloride Phenylhydrazones and Related Compounds

$$R_1-\underset{\underset{X}{|}}{C}=NNH-\under{}(Y)_n$$

Compound no.	R_1	X	$(Y)_n$	Herbicidal activity		
				10 lb/acre	3 lb/acre	1 lb/acre
2	CH₃CH₂–	Cl	2,4-Cl₂	10	a	a
3	CH₃CH₂–	Cl	2,4,6-Cl₃	7.0	8.7	7.6
40	CH₃CH₂CH₂–	Cl	2,4,6-Cl₃	9.9	8.9	5.4
41	(CH₃)₂CH–	Cl	2,4,6-Cl₃	9.9	a	a
42	(CH₃)₃C–	Cl	2,4,6-Cl₃	9.0	9.9	7.4
43	(CH₃)₃C–	Cl	2,5-Cl₂	5.8		
44	(CH₃)₃C–	Cl	Unsub	4.5		
45	(CH₃)₃C–	Cl	4-NO₂	0		
46	(CH₃)₃C–	Cl	2,4-(NO₂)₂	0		
47	(CH₃)₂CH–	CN	2,4,6-Cl₃	0		

[a] Tests at lower rates on other weed species showed these chemicals to be comparable to 3 in activity.

30, X = Cl
38, X = CH₃
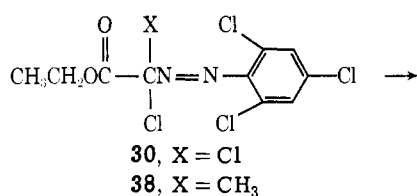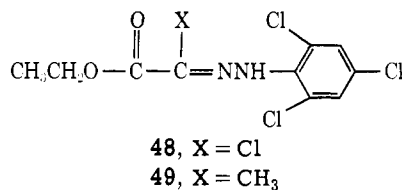
48, X = Cl
49, X = CH₃

phenyl)hydrazone] **(49)**. Whether these are chemical or biochemical transformations is not known at this time. These conversions, and also reduction of **4** to **3**, are readily effected chemically by catalytic hydrogenation using a 10% palladium–charcoal catalyst in ethyl acetate; reduction of **30** and **38** with sodium borohydride in ethanol is also rapid.

Additional studies will be needed to determine the possible significance and generality of the reduction of these azo compounds in plants and the mode of action of the herbicides described in this paper.

ACKNOWLEDGMENT

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