Syntheses and Herbicidal Activities of Dithiocarbamates

Part I. Benzyl Esters of N-Substituted Dithiocarbamic Acids and Related Compounds

By Shigeki WAKAMORI, Yoshio YOSHIDA and Yoshio ISHII

Research Laboratory, Toa Agricultural Chemicals Co., Ltd.,
Odawara, Kanagawa-Pref.*

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Several dithiocarbamates were synthesized and their herbicidal activities to radish and barnyardgrass were examined. Some benzyl N, N-dialkyldithiocarbamates such as N-methyl-N-ethyl-, N-methyl-N-n-propyl-, N, N-diethyl- and N, N-diisopropyl-dithiocarbamates showed high activity to these plants, but N-monoalkyl-, N, N-diaryl- and N, N-dialkyl-dithiocarbamates were not so active. Some substituted benzyl N, N-dialkyldithiocarbamates such as 4-dimethylaminobenzyl N-methyl-N-ethyldithiocarbamate and 4-methoxybenzyl N, N-diethyldithiocarbamate showed high activity to broad-leaved plants. Substituted benzyl N, N-dialkyldithiocarbamates except 4-cyanobenzyl N, N-diisopropyldithiocarbamate, however, were less active to graminaceous plants.

Antifungal^{1~3)} and miticidal⁴⁾ activities of the dithiocarbamates have already been reported by many investigators, and various dithiocarbamates are practically used as fungicides. On the other hand, the herbicidal activity of the dithiocarbamates, methyl, allyl and chloro-substituted benzyl N, N-diisopropyldithiocarbamates have also been reported by Harman,^{5,6)} Klingman,⁷⁾ and Hilton,⁸⁾ respectively. However, no systematic study on

the relationship between herbicidal activity and chemical structure has been reported yet so far. The authors systematically synthesized various dithiocarbamates in order to study the effect of changes in chemical structures of dithiocarbamates on herbicidal activity. Some dithiocarbamates prepared by the authors showed excellent herbicidal activity against graminaceous and broad-leaved plants.

MATERIALS AND METHODS

Infrared spectrum. Infrared spectra of the dithiocarbamates, measured with a Hitachi EPI-G spectrophotometer, are shown in Tables I and II.

Synthesis. Almost all of the dithiocarbamates were synthesized by reactions of sodium salts of dithiocarbamic acids and halogen compounds, R-Cl (R: methyl, allyl, cyanoethyl, benzyl, substituted benzyl, etc.) in acetone or alcohol. Phenyl ester of dithiocarbamic acid (VII in Table I) was synthesized from sodium dithiocarbamate and benzenediazonium chloride. The details of some typical procedures are given below. The physical constants and analytical data

* Present address: Chemical Research Laboratory, Kumiai Chemical Industry Co., Ltd., Shimizu, Shizuoka-Pref.

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8) H. W. Hilton and N. Nomura, *Weed Res.*, **4**(3), 216 (1964).

Continued from Table I

No.	R ₁	R ₂	R ₃	Yield %	bp °C/mmHg (mp °C)	$\bar{n}_d^{25}$ (solvent of recrystal- lization)	Formula	Calcd. N S	Found N S	IR-Absorption ν -N=C=S cm ⁻¹
XXXIV	C ₆ H ₅	C ₆ H ₅	C ₆ H ₅ CH ₂	49	(115~7)	(Hexane)	C ₂₀ H ₁₇ NS ₂	4.18 19.17	4.25 19.12	1495
XXXV	C ₆ H ₅ CH ₂	H	C ₆ H ₅ CH ₂	83	(71~2) ^(f)	(Hexane)	C ₁₅ H ₁₅ NS ₂	5.12 23.45	5.21 23.55	1500
XXXVI	C ₆ H ₅ CH ₂	C ₆ H ₅ CH ₂	C ₆ H ₅ CH ₂	68	(94~5)	(Hexane)	C ₂₂ H ₂₁ NS ₂	3.85 17.64	3.82 17.63	1480
XXXVII		NC(=S)SCH ₂ -		60	(52) ^(h)	(Ethanol)	C ₁₃ H ₁₇ NS ₂	5.57 25.51	5.72 25.61	1470
XXXVIII		NC(=S)SCH ₂ -		68	(69~70)	()	C ₁₂ H ₁₅ NOS ₂	5.53 25.31	5.50 25.01	1485
XXXIX	CH ₂ NHC(=S)SCH ₂ -	CH ₂ NHC(=S)SCH ₂ -		22	(128~9)	()	C ₁₈ H ₂₀ NS ₄	7.14 32.66	7.19 32.60	1495

a) Uncorrected.

b) Lit.^(b) not described physical constants.

c) A. Margot, [U.S. Patent, 3075875 (1963)] reported mp of 49~51°C.

d) Lit.⁽¹⁾ 40~1°C.

e) R. F. McCleary and J. E. Fields, [U.S. Patent, 2366539 (1945)] not described physical constants.

f) Lit.⁽¹⁾ not described physical constants.g) J. P. Trivedi and I. D. Shah, [*Indian J. Pharm.*, **25**, 421 (1963); *C.A.*, **60**, 13168 (1964)] reported mp of 64°C by other synthetic method.h) T. Takemoto, K. Daigo and M. Tanaka, [*Yakugaku Kenkyu*, **33**, 7 (1961)] reported mp of 50~2°C.

TABLE II. PHYSICAL CONSTANTS AND ANALYTICAL DATA OF THE SYNTHETIC COMPOUNDS

No.	R ₁	R ₂	R ₃	Yield %	mp °C ⁽¹⁾ (bp °C/mmHg)	n_D^{25} (solvent of recrystallization)	Formula	Calcd.		Found		IR-Absorption $\nu_{\text{N}=\text{C}=\text{S}}$ cm ⁻¹
								N	S	N	S	
							$\text{R}_1\text{--}\text{N}(\text{C}=\text{S})\text{CH}_2\text{--}\text{C}_6\text{H}_4\text{--}\text{R}_3$					
XL	CH ₃	CH ₃	4-Cl	72	53~4.5 ^{b)}	Petro. ether	C ₁₀ H ₁₂ ClNS ₂	5.70	26.09	5.80	26.21	1475
XLI	"	"	3,4-Cl ₂	80	77 ^{c)}	"	C ₁₀ H ₁₁ Cl ₂ NS ₂	5.00	22.88	5.02	23.00	1490
XLII	"	"	2,4-Cl ₂	79	88~90 ⁽¹⁾	"	"	"	"	5.30	22.95	1490
XLIII	"	"	2,3,4-Cl ₃	74	(138~40/0.05)	(1.6599)	C ₁₀ H ₁₀ Cl ₃ NS ₂	4.45	20.37	4.62	20.60	1490
XLIV	"	"	2,4,5-Cl ₃	75	117~8.5	Petro. ether	"	"	"	4.35	20.51	1490
XLV	"	"	4-CH ₃	82	85~7	"	C ₁₁ H ₁₃ NS ₂	6.22	28.45	6.33	28.59	1471
XLVI	"	"	4-NO ₂	92	108 ⁽¹⁾	Ligroin	C ₁₀ H ₁₂ N ₂ O ₂ S ₂	10.93	25.01	11.00	25.36	1475
XLVII	C ₂ H ₅	C ₂ H ₅	4-Cl	82	36	Petro. ether	C ₁₂ H ₁₆ ClNS ₂	5.12	23.42	5.40	23.60	1475
XLVIII	"	"	3,4-Cl ₂	81	(165~8/0.03)	(1.6172)	C ₁₂ H ₁₅ Cl ₂ NS ₂	4.54	20.80	4.70	21.02	1490
XLIX	"	"	2,4-Cl ₂	57	39~40	Petro. ether	"	"	"	4.81	21.10	1490
L	"	"	2,6-Cl ₂	95	87~8	"	"	"	"	4.52	20.96	1490
LI	"	"	2,3,4-Cl ₃	86	(180~3/0.03)	(1.6162)	C ₁₂ H ₁₄ Cl ₃ NS ₂	4.09	18.71	4.35	19.00	1490
LII	"	"	2,4,5-Cl ₃	91	74~6	Petro. ether	"	"	"	4.08	18.90	1490
LIII	"	"	2,3,6-Cl ₃	50	55~7 ⁽¹⁾	"	"	"	"	4.01	18.72	1490
LIV	"	"	4-CH ₃	99	(138~40/0.03)	(1.6056)	C ₁₃ H ₁₄ NS ₂	5.53	25.30	5.50	25.18	1471
LV	"	"	4-NO ₂	96	74~5	Ethanol	C ₁₂ H ₁₆ N ₂ O ₂ S ₂	7.97	18.23	8.01	18.60	1475
LVI	"	"	4-Br	82	53~4	Ligroin	C ₁₂ H ₁₅ BrNS ₂	4.40	20.14	4.32	20.02	1471
LVII	"	"	4-OCH ₃	49	65~7	"	C ₁₃ H ₁₈ NOS ₂	5.20	23.80	5.10	23.90	1470
LXVIII	"	"	4-CN	68	46~7	Hexane	C ₁₃ H ₁₆ N ₂ S ₂	10.60	24.25	10.52	24.38	1468
LIX ⁽¹⁾	<i>i</i> -C ₃ H ₇	<i>i</i> -C ₃ H ₇	2-Cl	91	(148~50/0.04)	(1.5865)	C ₁₄ H ₂₀ ClNS ₂	4.64	21.24	4.41	21.26	1470
LX ⁽¹⁾	"	"	3-Cl	70	57~9	Petro. ether	C ₁₄ H ₂₀ ClNS ₂	4.64	21.24	4.94	21.38	1470
LXI	"	"	4-Cl	80	88~9 ⁽¹⁾	"	"	"	"	4.54	21.50	1470
LXII	"	"	3,4-Cl ₂	30	70~1 ⁽¹⁾	"	C ₁₄ H ₁₉ Cl ₂ NS ₂	4.17	19.06	4.28	19.26	1460
LXIII	"	"	2,4-Cl ₂	88	(155~7/0.04)	(1.6048)	"	"	"	4.12	19.08	1460
LXIV	"	"	2,6-Cl ₂	82	107 ⁽¹⁾	Ligroin	"	"	"	4.15	19.40	1460
LXV ⁽¹⁾	"	"	2,3,4-Cl ₃	65	(178~9/0.02)	(1.6224)	C ₁₄ H ₁₈ Cl ₃ NS ₂	3.78	17.29	4.02	17.70	1480
LXVI	"	"	2,4,5-Cl ₃	65	55 ⁽¹⁾	Ligroin	"	"	"	4.00	17.10	"
LXVII	"	"	2,3,6-Cl ₃	63	86 ⁽¹⁾	"	"	"	"	3.62	17.39	"
LXVIII	"	"	2-Br	82	74~5	"	C ₁₄ H ₂₀ BrNS ₂	4.04	18.51	4.03	18.51	1467
LXIX	"	"	3-Br	78	77~8	"	"	"	"	4.16	18.72	"
LXX	"	"	4-Br	76	102~3	"	"	"	"	4.33	18.70	"
LXXI	"	"	2-J	72	92~3	"	C ₁₄ H ₂₀ JNS ₂	3.56	16.30	3.87	16.25	"
LXXII	"	"	3-J	86	96	"	"	"	"	3.85	16.06	"

Continued from Table II

No.	R ₁	R ₂	R ₃	Yield %	mp °C (bp °C/mmHg)	n_D^{25} (solvent of recrystallization)	Formula	Calcd. N S	Found N S	IR-Absorption $\nu_{N=C=S}$ cm ⁻¹
LXXXIII	i-C ₃ H ₇	i-C ₃ H ₇	4-J	54	107	Ligroin	C ₁₄ H ₂₀ INS ₂	3.56 16.30	3.49 16.69	1467
LXXXIV	"	"	2-CH ₃	66	60~1	Petro. ether	C ₁₅ H ₂₃ NS ₂	4.98 22.78	4.88 23.01	"
LXXV	"	"	3-CH ₃	60	59~60	"	"	" "	4.90 22.77	1461
LXXVI	"	"	4-CH ₃	73	65~6	"	"	" "	4.98 22.56	"
LXXVII	"	"	2-NO ₂	51	121~2	Ethanol	C ₁₄ H ₂₀ N ₂ O ₂ S ₂	8.97 20.52	9.05 20.68	1478
LXXVIII	"	"	3-NO ₂	29	150~1	"	"	" "	9.10 20.72	1472
LXXIX	"	"	4-NO ₂	70	84	"	"	" "	9.01 20.50	"
LXXX	"	"	2-CN	55	112	Ligroin	C ₁₃ H ₂₀ N ₂ S ₂	9.58 23.03	9.62 23.00	1468
LXXXI	"	"	3-CN	20	146	"	"	" "	9.56 23.32	"
LXXXII	"	"	4-CN	58	80~1	"	"	" "	9.59 23.20	"
LXXXIII	"	"	4-OCH ₃	63	75~6	"	C ₁₃ H ₂₀ NOS ₂	4.71 21.55	4.50 21.38	"
LXXXIV	CH ₃ C ₂ H ₅	"	4-N(CH ₃) ₂	62	80~2	Methanol	C ₁₃ H ₂₀ N ₂ S ₂	10.44 23.90	10.32 23.76	1473
LXXXV	"	"	4-Cl	60	49~50	Petro. ether	C ₁₁ H ₁₄ ClNS ₂	5.39 24.68	5.20 24.75	1478
LXXXVI	"	"	4-Br	85	71~2	"	C ₁₁ H ₁₄ BrNS ₂	4.60 21.07	4.38 20.95	1476
LXXXVII	"	"	4-CH ₃	72	30~2	"	C ₁₃ H ₁₇ NS ₂	5.85 26.78	5.72 26.49	1471
LXXXVIII	"	"	4-NO ₂	35	47~8	"	C ₁₁ H ₁₄ N ₂ O ₂ S ₂	10.36 23.71	10.25 23.72	1475
LXXXIX	"	"	4-OCH ₃	83	83~5	"	C ₁₂ H ₁₇ NOS ₂	5.49 25.10	5.42 25.10	1472
XC	CH ₃	n-C ₃ H ₇	4-Cl	91	39~41	Hexane	C ₁₂ H ₁₈ ClNS ₂	5.12 23.42	5.18 23.62	1478
XCI	"	"	4-CH ₃	84	(142~4/0.03)	(1.6009)	C ₁₃ H ₁₉ NS ₂	5.53 25.30	5.42 25.30	1476
XCV	"	"	4-NO ₂	32	35~6	Hexane	C ₁₃ H ₁₈ N ₂ O ₂ S ₂	9.85 22.54	9.72 22.30	1470
XCIII	"	"	4-CN	70	40.5	"	C ₁₃ H ₁₆ N ₂ S ₂	10.60 24.25	10.49 24.39	"

Uncorrected

- a) M. Kulka, [*Can. J. Chem.*, **34**, 1093 (1956)] reported mp of 54~5°C.
b) M. Kulka, [*Can. J. Chem.*, **34**, 1093 (1956)] reported mp of 75~6°C.
c) M. Kulka, [*Can. J. Chem.*, **34**, 1093 (1956)] reported mp of 82~3°C.
d) M. Kulka, [*Can. J. Chem.*, **34**, 1093 (1956)] reported mp of 106~7°C.
e) M. Kulka, [*Can. J. Chem.*, **34**, 1093 (1956)] reported bp of 202~3°C/0.3 mmHg.
f) J. S. Newcomer, [U.S. Patent, 3156645 (1964); *C.A.* **62**, 7696 (1965)] reported bp of 59~61°C.
g) Lit.⁶⁾ not described physical constants. h) Lit.⁶⁾ 84~5°C. i) Lit.⁶⁾ 59~61°C.
j) Lit.⁶⁾ 100~101°C. k) Lit.⁶⁾ 53~4°C. l) Lit.⁶⁾ 83°C.

of the synthetic compounds are presented in Tables I and II.

1) *Phenyl N, N-diisopropyldithiocarbamate (VII)*. To 10% aqueous solution containing 17.4 g of sodium N, N-diisopropyldithiocarbamate was added dropwise a solution of 9.5 g of benzenediazonium chloride in 50 ml of water at 40~50°C with vigorous stirring. After the addition of the diazonium chloride, the reaction mixture was stirred at 30~40°C for an additional 1 hr. The yellow solid thus formed was extracted with 100 ml of ether. The ether layer was washed successively with 5% sodium hydroxide, 10% sulfuric acid and several portions of water, and then dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was recrystallized from ethanol to give 10.8 g of pale yellow prisms, mp 135~136°C.

2) *Benzyl N, N-diisopropyldithiocarbamate (XXI)*. To a mixture of 10 g of sodium N, N-diisopropyldithiocarbamate and 100 ml of acetone was added dropwise 6.3 g of benzyl chloride at 30~35°C with stirring. After the addition, the reaction mixture was stirred at 30~35°C for additional 2 hr, and then acetone was evaporated. The residual oil was extracted with 100 ml of ether and washed with water. The ether was removed after drying over anhydrous sodium sulfate. The residue was distilled at 141~142.5°C (0.04 mm-Hg) to yield 13.1 g of an oil. The oil was recrystallized from petroleum ether to give crystals melting at 36°C. The IR spectrum of this compound is shown in Fig. 1.

FIG. 1. IR Spectra of Benzyl N, N-Dialkyldithiocarbamates.

- (1): N, N-diethyl compound (XV)
(2): N, N-diisopropyl compound (XXI)

3) *4-Dimethylaminobenzyl N-methyl-N-ethylthiocarbamate (LXXXIV)* To a solution of 6 g of sodium N-

methyl-N-ethylthiocarbamate in 50 ml of acetone was added dropwise a solution of 5.1 g of 4-dimethylaminobenzylchloride in 50 ml of acetone at 30~35°C. After the addition, the reaction mixture was stirred at 30~35°C for additional 2 hr, and acetone was removed. The residual oil was extracted with 100 ml of ether, and washed with several portions of water. The ether was removed after drying over anhydrous sodium sulfate. The residue was recrystallized from methanol to yield 4.9 g of pale yellow needles, mp 80~82°C.

Evaluation of herbicidal activities. Herbicidal activities were examined by using one-five thousand pots. Each pot was filled with alluvial loamy soil, in which germinated rice seeds were planted together with radish or barnyardgrass seeds and kept in a greenhouse at 30°C. After one day, emulsions containing definite amounts of test chemicals were sprayed. Air-dried weight of each plant was measured 30 days after treatment with the chemicals. The herbicidal activity was determined by the following equation:

$$\text{Inhibition percentage} = \left(1 - \frac{A}{B}\right) \times 100,$$

where A represents the air-dried weight of a plant treated with chemical, and B represents the air-dried weight of a plant treated with control solution. Inhibitory ratings are determined by the following rating system.

0 : 0~20% inhibition, 1 : 20~40% inhibition, 2 : 40~60% inhibition, 3 : 60~80% inhibition, 4 : 80% or higher inhibition, 5 : complete inhibition (Seedlings were killed after germination).

RESULTS AND DISCUSSION

The herbicidal activities of non-substituted and substituted benzyl dithiocarbamates are shown in Tables III and IV, respectively. Harman *et al.*⁵⁾ reported that alkyl or allyl esters of dithiocarbamic acids showed a moderate activity to graminaceous and broad-leaved plants. The result of the present investigation showed that methyl (I), hydroxycarbonylmethyl (VI), aminocarbonylmethyl (VIII), acetylmethyl (IV), hydroxyethyl (V) and phenyl (VII) esters of dithiocarbamic acids have no activity to radish and barnyardgrass. Allyl (II)

TABLE III. HERBICIDAL ACTIVITIES OF NON-SUBSTITUTED BENZYL DITHIOCARBAMATES

No.	$\Sigma\sigma^*$ value ^{a)}	Herbicidal activities						Phytotoxicity ^{b)}	
		Radish			Barnyardgrass			Rice	
		500	250	100	500	250	100	500	100 ^{c)}
I		0			0			0	0
II		0			5	2	0	0	0
III		0			5	3	0	3	0
IV		0			2	0		0	0
V		0			0			0	0
VI		0			0			0	0
VII		0			0			0	0
VIII		0			0			0	0
IX	0.490	1	1	0	4	2	0	1	0
X	0.000	5	3	2	5	3	2	3	1
XI	-0.100	5	5	5	5	5	5	0	0
XII	-0.115	5	5	4~5	5	5	4~5	0	0
XIII	-0.190	5	5	4	5	5	4	0	0
XIV	0.390	3	2	0	4	2	1	0	0
XV	-0.200	5	5	4	5	5	4	0	0
XVI	-0.290	5	5	3	5	4	3	0	0
XVII	-0.225	5	4	4	5	4	4	0	0
XVIII	0.375	3	3	1	4	3	1	0	0
XIX	-0.230	5	4	4	5	5	4	0	0
XX	0.300	2	1	1	3	3	2	0	0
XXI	-0.380	5	5	4	5	5	4	0	0
XXII	-0.315	5	3	3	5	4	3	0	0
XXIII	0.360	1	1	0	2	1	0	1	0
XXIV	-0.260	5	4	3	5	4	3~4	0	0
XXV	0.365	1	1	0	2	1	0	0	0
XXVI	-0.250	5	4	4	5	5	4	0	0
XXVII	0.190	2	0		2	0		2	0
XXVIII		2	1	0	4	2	0	0	0
XXIX		0			0			2	1
XXX		5	3	0	4	3	1	1	0
XXXI	0.34	0			0			0	0
XXXII	-0.30	0			0			0	0
XXXIII	1.090	0			0			0	0
XXXIV	1.200	0			0			0	0
XXXV	0.705	1	1	0	2	2	0	0	0
XXXVI	0.430	0			2	0		0	0
XXXVII		2	1	1	1	1	0	0	0
XXXVIII		2	0		1	1	0	1	0
XXXIX		0			0			3	1
PCP ^{d)}		5	4	3	5	4	3	0	0
Control		0			0			0	

a) Sum of the Taft's σ^* value.^{14, 15)}

b) Phytotoxic ratings are as follows:

0: no inhibition, 1: slight inhibition, 2: moderate inhibition 3: complete inhibition.

c) Dose (gram) per 10 are.

d) Sodium pentachlorophenolate.

TABLE IV. HERBICIDAL ACTIVITIES OF SUBSTITUTED BENZYL N, N-DIALKYL-DITHIOCARBAMATES

No.	Radish			Barnyardgrass			No.	Radish			Barnyardgrass		
	250	100	50	250	100	50		250	100	50	250	100	50 ^{a)}
XL	5	3	1	5	3	1	LXVIII	4	3	0	0	1	
XLI	5	3	0	5	3	0	LXIX	4	1	0	0		
XLII	0			0			LXX	4	2	0	2	0	
XLIII	4	0		4	1	0	LXXI	3	0		0		
XLIV	1	0		0			LXXII	3	0		0		
XLV	3	3	2	3	2	0	LXXIII	3	0		0		
XLVI	3	0		2	0		LXXIV	5	3	0	3	1	0
XLVII	5	4	1~2	3	1	0	LXXV	0			2	0	
XLVIII	0			0			LXXVI	5	5	3	5	2	0
XLIX	0			0			LXXVII	0			1	0	
L	0			0			LXXVIII	0			0		
LI	0			0			LXXIX	5	5	2	3	0	
LII	0			0			LXXX	5	5	4	5	2	0
LIII	0			0			LXXXI	0			0		
LIV	5	5	3	5	3	0	LXXXII	5	5	4	5	5	4
LV	3	2	0	2	1	0	LXXXIII	5	5	3~4	0		
LVI	5	3	1~2	2	1	0	LXXXIV	5	5	4	3	0	
LVII	5	5	4	3	0		LXXXV	5	4	1	1	0	
LVIII	3	1	1	1	0		LXXXVI	5	3	1	1	0	
LIX	5	3	2	3	0		LXXXVII	5	5	3	5	3	1
LX	5	2	0	3	0		LXXXVIII	3	1	0	0		
LXI	5	4	1	3	0		LXXXIX	5	4	3	1	1	0
LXII	4	3	0	1	0		XC	5	4	2	1	0	
LXIII	4	1	0	0			XCI	5	5	3~4	1	1	0
LXIV	4	2	1	0			XCI	5	4	0	1	0	
LXV	3	0		2	0		XCI	3	1	0	0		
LXVI	3	0		2	0		PCP ^{b)}	4	3	0	4	3	1
LXVII	3	2	0	2	0		Control	0			0		

a) Dose (gram) per 10 are.

b) Sodium pentachlorophenolate.

or cyanoethyl(III) esters were not active to radish but highly active to barnyardgrass at a dosage of 500 g per 10 are. The activity of allyl or cyanoethyl esters, however, were much less than that of benzyl esters. Among the benzyl esters, morpholyl-(XXXVII), piperidyl-(XXXVIII), N, N-diallyl-(XXX), N, N-dicyclohexyl-(XXXII), N, N-diphenyl-(XXXIV), N, N-dibenzyl-(XXXVI), and N-mono-substituted-dithiocarbamates were weakly active to radish or barnyardgrass. But some benzyl N, N-dialkyldithiocarbamates, especially, N-methyl-N-ethyl-(XI), N-methyl-N-n-propyl-(XII),

N-methyl-N-isopropyl-(XIII), N, N-diethyl-(XV), and N, N-diisopropyl-(XXI) dithiocarbamates showed higher activity to both plants. These compounds were non-selective between graminaceous and broad-leaved plants. As shown in Table III, the herbicidal activity of benzyl N, N-dialkyldithiocarbamates increased in the order: N-methyl-N-ethyl $\geq$ N-methyl-N-n-propyl > N-methyl-N-isopropyl, N, N-diethyl, N, N-diisopropyl, N-ethyl-N-isobutyl, N, N-di-n-propyl, N, N-diisobutyl $\geq$ N, N-di-n-butyl > N-ethyl-N-isopropyl, N-isopropyl-N-isobutyl > N, N-dimethyl.

TABLE V. ACTIVITIES OF 4-SUBSTITUTED BENZYL N, N-DIALKYL-DITHIO-CARBAMATES AND THEIR HAMMETT'S σ CONSTANTS^{16, 17)}

$$\begin{array}{c} \text{R}_1 \quad \text{S} \\ \diagup \quad | \\ \text{N} \text{---} \text{C} \text{---} \text{S} \text{CH}_2 \text{---} \diagdown \\ \diagdown \quad | \\ \text{R}_2 \end{array} \quad \text{---} \quad \text{---} \text{R}_3$$

R ₃	σ value ^{16, 17)}	Herbicidal activities to radish								
		R ₁ R ₂	CH ₃ C ₂ H ₅		CH ₃ <i>n</i> -C ₃ H ₇		C ₂ H ₅ C ₂ H ₅		iso-C ₃ H ₇ iso-C ₃ H ₇	
			100	50	100	50	100	50	100	50 ^{a)}
N(CH ₃) ₂	-6.00		5	4	—	—	—	—	—	—
OCH ₃	-0.268		4	3	—	—	5	4	5	3~4
CH ₃	-0.170		5	3	5	3~4	5	3	5	3
H	0.000		5	2	4~5	3	4	3	4	3
Cl	0.227		4	1	4	2	4	1~2	4	1
Br	0.232		3	1	—	—	3	1~2	2	0
J	0.276		—	—	—	—	—	—	inactive	
CN	0.628		—	—	1	0	1	1	5	4
NO ₂	0.778		1	0	4	0	2	0	5	2

a) Dose (gram) per 10 are.

On the herbicidal activities of dichloro- or trichloro-benzyl N, N-diisopropylthiocarbamates, Harman *et al.*⁶⁾ and Klingman⁷⁾ reported that non-substituted benzyl ester was inactive, but that chloro-substituted benzyl esters were active. As shown in Table IV, introduction of various substituents into the aromatic ring of benzyl N, N-dialkylthiocarbamates decreased the herbicidal activity to graminaceous plants. For example, the herbicidal activity was decreased by the substitution of the halogen atom in the order of iodine > trichloro > bromine, dichloro > monochloro. But 4-cyanobenzyl N, N-diisopropylthiocarbamate (LXXXII) showed much higher activity to barnyardgrass.

On the other hand, the activity to broad-leaved plants was increased by the substitution at the 4-position of the benzyl group with dimethylamino, methoxy, or methyl groups. For example, 4-dimethylaminobenzyl N-methyl-N-ethylthiocarbamate (LXXXIV), 4-methoxybenzyl N, N-diethylthiocarbamate (LVII) and 4-methylbenzyl N-methyl-N-*n*-propylthiocarbamate (XCI) showed high activity. But the herbicidal activity was markedly

reduced by introduction of various substituents into 2- or 3-positions. Thus, it is suggested that the selectivity between graminaceous and broad-leaved plants is due to the various substituents introduced into the aromatic ring of benzyl N, N-dialkylthiocarbamates.

Recently, in order to explain the correlation of the biological activity to chemical structure, Hammett's δ constant, oil-water partition coefficient and p*K*_a-value were applied by several investigators.^{9~13)} As shown in Tables IV and V, N-mono-substituted dithiocarbamates and N, N-diphenyl- or N, N-dibenzyl-dithiocarbamates where $\Sigma\delta^*$ (sum of Taft's δ^* value^{14,15)} values of the N-alkyl substituents are positive

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scarcely showed activity to graminaceous and broad-leaved plants, but the N, N-dialkyldithiocarbamates having negative value were highly active to both plants. The introductions of dimethylamino, methoxy and methyl groups into the aromatic ring having negative δ values (Hammett's δ constant^{16,17)} were favorable to the activity, but those of the halogen atom and the nitro group having positive values brought about low activity. Thus, it might be suggested that the electronic property of the molecule is related to the herbicidal activity to some extent. As mentioned above, benzyl N, N-dialkyldithiocarbamates showed

a strong selectivity between barnyardgrass and rice plants, and it is important in practical use that these compounds are harmless to rice plants. The mammalian toxicities of benzyl N, N-diethyldithiocarbamate and benzyl N, N-diisopropyldithiocarbamate are very low, the acute oral LD₅₀ to mice being more than 2500 mg/kg. The toxicity of these compounds to carp-fish was not so high as Tlm 2.3~2.5 ppm after 48 hr.

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