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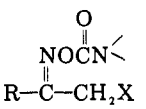
Insecticidal Substituted 2-Butanone *O*-(Methylaminocarbonyl)oximes

Thomas A. Magee* and Lawrence E. Limpel

Certain *N*-methylcarbamates derived from oximes of 3,3-dimethyl-2-butanones, with electronegative substituents on carbon 1, have demonstrated a broad spectrum of insecticidal and acaricidal activity similar or superior to that of earlier reported aldoxime derivatives. The preparation and pesticidal activity of over 40 ketoxime carbamates is reported. Structural requirements for high activity in the series are narrow. The most active compound, 3,3-dimethyl-1-(methylthio)-2-butanone *O*-[(methylamino)-carbonyl]oxime, is undergoing extensive field testing under the designations DS-15647 and thiofanox.

Since the initial account of the insecticidal properties of oxime carbamates (Kilsheimer and Manning, 1963), the several reports of this class of compounds have emphasized that it is primarily the aldoxime derivatives which exhibit high insecticidal activity (Weiden, 1968; Fukuto et al., 1969; Fridinger et al., 1971; Friedman and Gemrich, 1971; Durden and Weiden, 1974; cf. last reference for a recent review of the literature). We now wish to report a group of ketoxime carbamates of the type:



certain of which have excellent activity as contact and systemic insecticides.

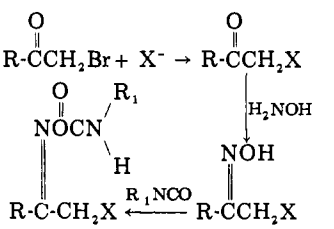
CHEMISTRY

The chemistry involved in the synthesis of these compounds is, for the most part, straightforward. Two general routes were followed. In the first (synthesis route A, Scheme I), an α-haloketone is treated with the appropriate nucleophile. The resulting substituted ketone is converted to the oxime and the carbamate by standard methods.

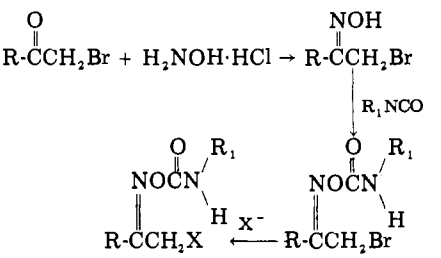
In the second route (synthesis route B), the haloketone is converted to the halooxime by treatment with hydroxylamine hydrochloride in the absence of base. Preparation of the carbamate and subsequent displacement of the halogen are then carried out by standard methods. A few of the ketones (Table IX) were prepared by other routes described in the literature.

The ketoxime carbamates may, of course, exist in the syn and anti forms. The configuration of the compounds has not been unequivocally established. The NMR

Scheme I



Synthesis route A



Synthesis route B

spectrum indicates that compound **5** (DS-15647, thiofanox), prepared by route A is a single isomer in which the carbamate moiety is thought to be anti to the *tert*-butyl group. A mixture containing nearly equal amounts of each isomer of the same compound was obtained by changing the sequence of steps in the synthesis. Treatment of the oxime of 1-bromopinacolone with sodium thiomethoxide afforded a mixture of the syn–anti isomers of 1-methylthiopinacolone oxime which was then converted to the carbamate mixture by reaction with methyl isocyanate.

The carbamate sulfides were oxidized to the corresponding sulfoxides and sulfones by well-known methods, using sodium periodate and peracetic acid, respectively.

A few of the carbamates were obtained as viscous oils which could not be obtained analytically pure; the physical properties and elemental analyses of the remaining carbamates are given in Table I. The structure of each compound was established by its infrared spectrum, and,

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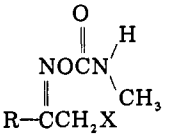
Table I. Physical Properties of Carbamates



Compd no.	R	X	Route employed	Mp, °C (refractive index/°C)	Analysis					
					Calculated, %			Found, %		
					C	H	N	C	H	N
1	CH_3-	CH_3S-	A	47-50	40.9	6.9		40.8	6.7	
2	CH_3CH_2-	CH_3S-	A	(1.5050/24)			14.7			15.0
3	$CH_3CH_2CH_2$-	CH_3S-	A	(1.5030/24)	47.0	7.9	13.7	46.8	7.9	13.9
4	$(CH_3)_2CH$-	CH_3S-	A	(1.5015/24)			13.7			13.5
5[a]	$(CH_3)_3C$-	CH_3S-	A	57-58	49.5	8.3	13.0	49.6	8.2	13.2
6	$(CH_3)_3CCH_2$-	CH_3S-	A	(1.4960/23)	51.7	8.7		51.3	8.5	
7	c-C_3H_5	CH_3S-	A	(1.5297/23)			13.9			14.3
8	c-1-$C_3H_5CH_3$	CH_3S-	A	(1.5220/24)	50.0	7.5		49.7	7.5	
9	$CH_3CH_2(CH_3)_2C$-	CH_3S-	A	(1.5030/23)	51.7	8.7		51.4	8.5	
10	$CH_3CH_2CH_2(CH_3)_2C$-	CH_3S-	A	(1.4937/24)			11.4			11.5
11	1-$CH_3C_6H_{10}$-	CH_3S-	A	(1.5200/25)	55.8	8.6		55.7	8.6	
12	$CH_3S(CH_3)_2C$-	CH_3S-	A	(1.5339/24)	43.2	7.2	11.2	43.2	7.4	11.3
13	$(CH_3)_3C$-	$CH_3S(O)$-		78-79	46.1	7.7	12.0	46.2	7.7	12.4
14	$(CH_3)_3C$-	CH_3SO_2-		69-70	43.2	7.3	11.2	43.3	7.2	11.0
15	$(CH_3)_3C$-	CH_3CH_2S-	A	50-51	51.7	8.7	12.2	51.4	8.9	12.2
16	$(CH_3)_3C$-	$CH_3CH_2CH_2S$-	A	68-70	53.6	9.0	11.4	53.2	9.1	11.4
17	$(CH_3)_3C$-	$(CH_3)_2CHS$-	A	63-64	53.6	9.0		53.6	8.5	
18	$(CH_3)_3C$-	$CH_2=CHCH_2S$-	A	(1.5075/25)			11.5			11.9
19	$(CH_3)_3C$-	$CH_3SCH_2CH_2S$-	B	61-62	47.5	8.0	10.1	47.2	8.2	10.1
20	$(CH_3)_3C$-	C_6H_5S-	A	108-109	60.0	7.2	10.0	60.0	7.4	10.2
21	$(CH_3)_3C$-	C_6H_5-SO_2-		157-159	53.8	6.5	9.0	53.3	6.3	9.0
22	$(CH_3)_3C$-	$CH_3OC(O)CH_2S$-	A	(1.5016/24)	47.8	7.3		48.0	7.6	
23	$(CH_3)_3C$-	$CH_3C(O)S$-	B	53-57	48.8	7.4	11.4	48.3	7.5	11.8
24	$(CH_3)_3C$-	NCS-	B	85-86	47.1	6.6		47.5	6.6	
25	$(CH_3)_3C$-	CH_3O-	A	(1.4650/24)	53.4	9.0		52.8	9.0	
26	$(CH_3)_3C$-	CH_3CH_2O-	A	(1.4649/25)			13.0			13.1
27	$(CH_3)_3C$-	C_6H_5O-	A	128-129	63.6	7.6	10.6	63.7	7.7	10.7
28	$(CH_3)_3C$-	$CH_3C(O)O$-	B	48-50	52.1	7.9	12.2	51.8	7.8	12.4
30	$(CH_3)_3C$-	CH_3SO_2O-		(1.4810/25)			10.5			10.5
31	$(CH_3)_3C$-	$(CH_3)_2N$-	B	42-43			19.5			19.3
32	$(CH_3)_3C$-	$(CH_3)_2N$-HCl	B	137-138	47.7	8.8	16.7	47.7	8.8	16.7
33	$(CH_3)_3C$-	NO_2-	A	59-61	44.2	7.0	19.4	44.7	7.3	19.6
34	$(CH_3)_3C$-	N_3-	B	67-68	45.1	7.1		45.2	7.3	
35[b]	$(CH_3)_3C$	H-	A	45-46	55.8	9.4		55.8	9.1	
36[b]	$CH_3S(CH_3)_2C$-	H-	A	79						
37	$(CH_3)_3C$-	CH_3SCH_2-	A	56-58	51.7	8.7		51.6	8.5	
38	$(CH_3)_3CC(=NOCONHCH_3)CH(SCH_3)CH_3$		A	93-94	51.7	8.7	12.1	51.6	8.5	12.1
39	$(CH_3)_3CC(=NOCONHCH_3)$-1-$CH(CH_2S)S$-1		A	83-86	45.8	6.9		45.6	6.9	
40[c]1	$(CH_3)_3C$-	CH_3S-	A	(1.5010/25)	49.5	8.3	13.0	49.2	8.0	12.7
41	$(CH_3)_3CC(=NOCONH_2)CH_2SCH_3$		C	58-60	47.0	7.9	13.7	46.7	7.7	13.5
43	$(CH_3)_3CC(=NOCON(H)CH_2CH=CH_2)CH_2SCH_3$		A	(1.5217/24)			11.5			11.2
44	$(CH_3)_3CC(=NOCON(CH_3)_2)CH_2SCH_3$		C	(1.4953/24)	51.7	8.7	12.1	51.6	8.5	11.8
	$(CH_3)_3C$-	Cl-	A	77-78			13.6			13.7
	$(CH_3)_3C$-	Br-	A	83-84	38.3	6.0	11.2	38.5	6.0	11.4

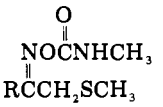
[a] Single isomer. [b] Payne et al. (1966). [c] Mixed isomers.

in some cases, by its NMR spectrum.

BIOLOGICAL TESTING

The compounds were screened for insecticidal or acaricidal activity against five species: Mexican bean beetle larvae (*Epilachna varivestis*), Southern armyworm larvae (*Spodoptera eridania*), adult housefly (*Musca domestica*), two-spotted spider mite (*Tetranychus urticae*), and black bean aphid (*Aphis fabae*). Contact activity was determined against all five; systemic activity against the mite and aphid was also measured. The fly, mite, and aphid were sprayed directly; the beetle and armyworm

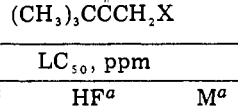
Table II. Effect of Variation in R on Biological Activity



Compd no.	R	LC_{50}, ppm					LC_{50}, lb/acre		I_{50}, m/L × 10^6
		BB[a]	AW[a]	HF[a]	M[a]	A[a]	MS[a]	AS[a]	
1	CH_3-	>500	>500	28	>500	58	>16	2.8	
2	CH_3CH_2-	>500	>500	100	>500	13	>16	1.95	
3	$CH_3CH_2CH_2$-	>500	>500	470	>500	8.6	>16	1.65	110
4	$(CH_3)_2CH$-	145	>500	90	300	13	>8	1.5	4.9
5	$(CH_3)_3C$-	26	280	170	9	1.4	0.51	0.09	5.4
6	$(CH_3)_3CCH_2$-	>500	>500	>500	130	28	>8	3.2	140
7	c-C_3H_5-	54	340	140	135	18	>8	3.2	16
8	c-1-$C_3H_5CH_3$-	45	>500	280	20	23	1.35	0.38	4.9
9	$CH_3CH_2(CH_3)_2C$-	26	>500	>500	15	4.2	0.75	1.1	2.6
10	$CH_3CH_2CH_2(CH_3)_2C$-	22	>500	>500	5.5	19	8.4	5.3	2.6
11	1-$(CH_3)C_6H_{10}$-	350	>500	>500	180	230	>8	>8	11
12	$CH_3S(CH_3)_2C$-	64	>500	500	31	15	>8	>8	2.2

[a] BB = Mexican bean beetle; AW = southern armyworm; HF = housefly; M = two-spotted spider mite; A = bean aphid; MS = mite systemic; AS = aphid systemic.

Table III. Effect of Variation in X on Biological Activity: I. X = $S(O)_nR$



Compd no.	X	LC_{50}, ppm					LC_{50}, lb/acre		I_{50}, m/L × 10^6
		BB[a]	AW[a]	HF[a]	M[a]	A[a]	MS[a]	AS[a]	
5	CH_3S-	26	280	170	9	1.4	0.51	0.09	5.4
13	$CH_3S(O)$-	13	420	180	23	3.3	1.1	0.25	4.8
14	CH_3SO_2-	6	>500	125	14	3.2	0.37	0.24	3.6
15	CH_3CH_2S-	94	>500	80	92	13	>8	1.32	3.6
16	$CH_3CH_2CH_2S$-	185	>500	220	170	54	>8	5.3	
17	$(CH_3)_2CHS$-	180	>500	170	>500	86	>16	3.3	
18	$CH_2=CHCH_2S$-	45	>500	78	78	55	>8	2.7	8.7
19	$CH_3SCH_2CH_2S$-	9.5	>500	440	54	36	>8	>8	1.3
20	C_6H_5S-	21	>500	420	>500	330	>16	>8	1.9
21	$C_6H_5SO_2$-	4.8	>128	>128	52	36	>4	>4	
22	$CH_3OC(O)CH_2S$-	86	>500	>500	400	16	>8	>8	
23	$CH_3C(O)S$-	86	>500	>500	>500	370	>16	>8	1.5
24	NCS-	48	>500	>500	>500	205	>16	>8	0.066

[a] BB = Mexican bean beetle; AW = southern armyworm; HF = housefly; M = two-spotted spider mite; A = bean aphid; MS = mite systemic; AS = aphid systemic.

larvae were placed onto previously sprayed leaf surfaces.

Anticholinesterase activity against bovine erythrocyte cholinesterase was determined using a colorimetric method for establishing the percent inhibition (Simpson et al., 1964).

DISCUSSION

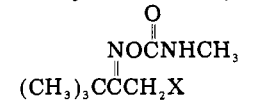
The insecticidal–acaricidal activity of these compounds exhibits the species variability typical of carbamates. In general, they show good to excellent activity against the Mexican bean beetle and the aphid, spotty activity against the mite, moderate to poor activity against the housefly, and little activity against the southern armyworm. With a few exceptions, they show activity against the rootknot nematode only at levels of 8 lb/acre or greater.

Four parts of the basic structure have been varied in the synthesis effort: R, X, the carbamate nitrogen substitution, and, in a few cases, the α-methylene group. The effects of some of these variations on the biological activity will be discussed.

When X is methylthio, extending the chain length of R (Table II) results in a moderately active aphicide with the *n*-propyl compound **3**, but little other results of interest. Branching at the α carbon has a more dramatic effect with maximum activity given by the fully branched compound **5**. The marked effect of small changes in molecular dimensions in this series may be seen with the 1-methylcyclopropyl compound **8** which is much less active than the *tert*-butyl analogue **5**. Branching at the β carbon has little beneficial effect (**6**). One of the substituents on the α carbon can be extended beyond methyl with only moderate loss in contact activity, although systemic activity is sharply lowered as the chain is lengthened (**9** and **10**). Incorporation of two of the substituents in a cyclohexyl ring (**11**) also lowers the activity. Replacement of a methyl by a methylthio group (**12**) lowers the contact activity and essentially abolishes the systemic effects. In greenhouse testing, this compound controlled the rootknot nematode at a rate of less than 0.5 lb/acre; field results were erratic.

Modification of X (Tables III and IV) gives results which emphasize both the species variability and the critical effect of structure on activity common to carbamate insecticides. In those cases where X is S-alkyl, increasing the size of the alkyl group tends to lower the activity, although there are exceptions on certain species. Oxidation of the sulfur results in an increase both in anticholinesterase activity and toxicity to the bean beetle; other

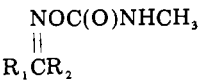
Table IV. Effect of Variation in X on Biological Activity: II. X=OR, NR

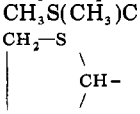
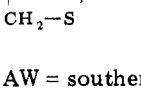


Compd no.	X	LC_{50} ppm BB[a]	AW[a]	HF[a]	M[a]	A[a]	LC_{50} lb/A MS[a]	AS[a]	I_{50}, m/L × 10^6
25	CH_3O-	185	>500	>500	>500	>500	>16	7	1.0
26	CH_3CH_2O-	220	>500	310	>500	>500	>16	>16	
27	C_6H_5O-	>500	>500	>500	>500	>500	>16	>16	10.0
28	$CH_3C(O)O$-	>500	>500	>500	>500	>500	>16	>16	
29	$CH_3NHC(O)O$-	240	>500	>500	>500	325	>16	5.8	
30	CH_3SO_2O-	>500	>500	>500	>500	>500	>16	>16	3.0
31	$(CH_3)_2N$-	>500	>500	>500	>500	>500	>16	>16	19
32	$(CH_3)_2N$·HCl	>500	>500	>500	>500	290	>16	>16	
33	NO_2-	>500	>500	>500	40	50	>16	>16	
34	N_3-	7.7	240	130	105	8.5	2.8	0.43	5.4

[a] BB = Mexican bean beetle; AW = southern armyworm; HF = housefly; M = two-spotted spider mite; A = bean aphid; MS = mite systemic; AS = aphid systemic.

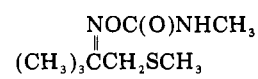
Table V. Biological Activity of Miscellaneous Carbamates



Compd no.	R_1	R_2	LC_{50}, ppm BB[a]	AW[a]	HF[a]	M[a]	A[a]	LC_{50}, lb/acre MS[a]	AS[a]	I_{50}, m/L × 10^6
35	$(CH_3)_3C$-	CH_3	>128	>128	>128	>128	>128	>4	>4	250
36	$CH_3S(CH_3)_2C$-	CH_3	500	>500	360	360	210	>8	5.3	
37	$(CH_3)_3C$-	$CH_3SCH_2CH_2$–	>500	>500	480	87	115	>8	>8	46
38	$(CH_3)_3C$-		440	>500	>500	>500	55	>16	1.65	100
39	$(CH_3)_3C$-		135	>500	500	>500	155	>16	>8	5.2
Aldicarb			38	>128	7.5	32	1.3	0.68	0.014	

[a] BB = Mexican bean beetle; AW = southern armyworm; HF = housefly; M = two-spotted spider mite; A = bean aphid; MS = mite systemic; AS = aphid systemic.

Table VI. Effect of Isomerism on Biological Activity



Compd no.	x	LC_x ppm BB[a] 50	95	AW[a] 50	95	HF[a] 50	95	M[a] 50	95	A[a] 50	95	LC_{50}, lb/acre MS[a] 50	95	AS[a] 50	95	I_{50}, m/L × 10^6
5	Single isomer	26	46	280	380	170	380	9	28	1.4	3.5	0.51	1.27	0.09	0.32	5.4
40	1:1 Mixed isomers	31	50	310	500	260	660	23	210	1.35	175	1.35	2.9	0.064	0.23	3.3

[a] BB = Mexican bean beetle; AW = southern armyworm; HF = housefly; M = two-spotted spider mite; A = bean aphid; MS = mite systemic; AS = aphid systemic.

insecticidal activity is variable (**5**, **13**, and **14**; **20** and **21**). This is in contrast to aldicarb where further oxidation of the sulfoxide to the sulfone lowers the insecticidal and anticholinesterase activity (Payne et al., 1966).

Wider modification of X emphasizes again the critical effect of structure. Only the azido compound **34** shows high insecticidal activity. The nitro compound **33** is chemically unstable; its intrinsic activity is probably somewhat higher. Efforts to prepare the corresponding cyano analogue have thus far been unsuccessful. The essential inactivity of the methoxy compound **25** is surprising in view of its anticholinesterase activity together with the reported insecticidal activity of the methoxy analogue of aldicarb (Payne et al., 1966)

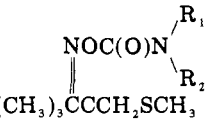
Placing the methylthio group one carbon further removed from the azomethine carbon (**37**) or substituting the methylene group (**38**) markedly lowers both the anticholinesterase and insecticidal activity (Table V).

The effect of isomerism on the insecticidal activity can be estimated by comparison of the single isomer with the 1:1 isomer mixture (Table VI). At the 50% control level, the differences are not striking; at the 95% control level, the single isomer is clearly superior, especially as a contact insecticide.

Variation of the substituents on the carbamate nitrogen gave the anticipated results with the monomethyl compound being by far the most active (Table VII). It is perhaps somewhat surprising that the unsubstituted carbamate shows the second highest activity of the group.

In keeping with their high anticholinesterase activity, these compounds have exhibited significant mammalian toxicity (Table VIII). Other analogues tested have also

Table VII. Effect of Carbamate Nitrogen Substitution on Biological Activity



Compd no.	R_1	R_2	LC_{50}, ppm BB[a]	AW[a]	HF[a]	M[a]	A[a]	LC_{50}, lb/acre MS[a]	AS[a]	I_{50}, m/L × 10^6
41	H-	H	38	>500	>500	50	8	3.5	1.0	2.2
5	CH_3-	H	26	280	170	9	1.4	0.51	0.09	5.4
42	CH_3CH_2-	H	130	>500	90	120	11	5.5	1.65	
43	CH_2=$CHCH_2$-	H	29	>500	360	140	18	5.5	2.7	
44	CH_3-	CH_3	>500	>500	>500	350	30	>8	1.1	98

[a] BB = Mexican bean beetle; AW = southern armyworm; HF = housefly; M = two-spotted spider mite; A = bean aphid; MS = mite systemic; AS = aphid systemic.

Table VIII. Mammalian Toxicity of Selected Carbamates

Compd no.	LD_{50} oral in mg/kg (rat)[a]	LD_{50} dermal in mg/kg (rabbit)[a]
5	8.5	38.9
13	3.8	178
14	1.9	60.3

[a] Mortalities determined 14 days after dosing.

been toxic to mice. Due precaution should be used in handling any of these carbamates.

As yet, clear-cut structure–activity correlations which will explain all of these results have not been drawn. The high activity of the 1-methylthio compound **5** compared with the essential inactivity of the 3-methylthio-2-butanone derivative **36** is difficult to explain. The insecticidal properties of the compounds are believed to be due to inhibition of cholinesterase and the analogies to acetyl choline employed by Payne et al. (1966) in their work on aldicarb may be applicable here also. However, their explanation (Payne et al., 1966; Durden and Weiden, 1974), on steric and electronic grounds, of the inactivity of **36** vs. aldicarb appears unable to account for the high activity of **5**. Additional work will be required to unravel the structure–activity relationship.

Compound **5** has undergone extensive field testing as a systemic insecticide under the code designation DS-15647. Advanced development work with this compound, now named thiofanox, is continuing.

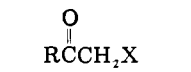
EXPERIMENTAL SECTION

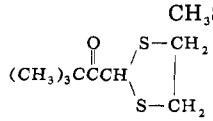
Chemical. Infrared spectra were determined on a Perkin-Elmer Model No. 137 spectrophotometer with sodium chloride optics. Nuclear magnetic resonance spectra were recorded on a Varian A56/60 spectrometer using tetramethylsilane as an internal standard. Melting points were determined on a Thomas-Hoover capillary melting apparatus and are uncorrected.

Representative examples of each procedure are given below; properties of specific compounds are listed in Table I, IX, and X. The 1-bromo- and 1-chloro-3,3-dimethyl-2-butanones were prepared by reported procedures (Boyer and Straw, 1952; Rabjohn and Rogier, 1946).

3,3-Dimethyl-1-(methylthio)-2-butanone. To a solution of sodium ethoxide prepared from 7.7 g (0.33 g-atom) of sodium metal and 200 mL of absolute ethanol was added

Table IX. Physical Properties of Ketone



R	X	Boiling range in °C/mmHg (melting range in °C)	Analysis Calculated C	Calculated H	Found C	Found H
CH_3-[a]	CH_3S-	63-64/29				
CH_3CH_2-	CH_3S-	50/5	50.8	8.5	50.7	8.5
$(CH_3)_2CH$-	CH_3S-	61/8	54.6	9.1	54.9	9.7
$(CH_3)_3C$-[b]	CH_3S-	73/9.3				
c-C_3H_5-	CH_3S-	71-74/7.8	55.4	7.7	55.6	7.9
$CH_3CH_2CH_2(CH_3)_2C$-	CH_3S-	59/0.2	62.0	10.4	62.3	10.7
1-$CH_3C_6H_{10}$-	CH_3S-	86-87/0.8	64.5	9.7	64.0	9.6
$CH_3S(CH_3)_2C$-	CH_3S-	91-95/3.9	47.2	7.9	46.8	7.8
$(CH_3)_3C$-	$CH_3CH_2CH_2S$-	49/0.3	62.0	10.4	61.7	10.3
$(CH_3)_3C$-	$(CH_3)_2CHS$-	96/8.9	62.0	10.4	61.8	10.2
$(CH_3)_3C$-	H_2C=$CHCH_2S$-	58-59/1.2	62.7	9.4	62.8	9.1
$(CH_3)_3C$-[c]	C_6H_5S-	102/0.5				
$(CH_3)_3C$-	$CH_3OC(O)CH_2S$-	94/0.8	52.9	7.9	52.6	7.5
$(CH_3)_3C$	NCS-	(35-37)	53.5	7.1	53.4	7.0
$(CH_3)_3C$-[d]	CH_3O-	78/47	64.5	10.8	64.3	10.8
$(CH_3)_3C$-[c]	C_6H_5O-	106-108/1.8				
$CH_3S(CH_3)_2C$-	H-	48/8.1	54.5	9.2	54.2	9.2
$(CH_3)_3C$-	CH_3SCH_2-	70/1.6	59.9	10.1	60.1	10.0
		(39-41)	50.5	7.4	51.1	7.4

[a] Cain and Cunneen (1962). [b] Asinger et al. (1958). [c] Leonard and Gelfand (1955). [d] Newman and Beal (1950).

Table X. Physical Properties of Oximes

$$RC(=NOH)CH_2X$$

R	X	Melting range in °C (refractive index/°C)	Analysis: Calculated C	Calculated H	Calculated N	Found C	Found H	Found N
CH_3-	CH_3S-	(1.5150/24)	40.3	7.6		40.7	7.6	
$CH_3CH_2CH_2$-	CH_3S-	(1.5010/24)	49.0	8.9	9.5	49.0	8.9	9.3
$(CH_3)_3C$-[a]	CH_3S-	b. 83 °/0.6 mmHg	52.1	9.4	8.7	52.2	9.4	8.6
$(CH_3)_3C$-[b]	CH_3S-	b. 79°/0.4 mmHg			8.7			8.5
c-C_5H_9-	CH_3S-	(1.5340/23)			9.7			9.5
$CH_3CH_2(CH_3)_2C$-	CH_3S-	b. 95°/0.7 mmHg	54.8	9.8		54.4	9.7	
$CH_3CH_2CH_2(CH_3)_2C$-	CH_3S-	(1.4863/24)			7.4			7.4
1-$CH_3C_6H_{10}$-	CH_3S-	(1.5164/24)	59.7	9.5	7.0	59.8	9.5	7.0
$CH_3S(CH_3)_2C$-	CH_3S-	70-75			7.2			6.8
$(CH_3)_3C$-	$CH_3S(O)$-	104-106	47.4	8.5	7.9	47.3	8.3	7.9
$(CH_3)_3C$-	CH_3SO_2-	81-82	43.5	7.8	7.3	43.3	7.8	7.1
$(CH_3)_3C$-	CH_3CH_2S-	71-72			8.0			7.9
$(CH_3)_3C$-	$CH_3CH_2CH_2S$-	(1.4879/24)			7.4			7.3
$(CH_3)_3C$-	$(CH_3)_2CHS$-	51-52			7.4			7.4
$(CH_3)_3C$-	$H_2C{=}CHCH_2S$-	57-58			7.5			7.3
$(CH_3)_3C$-	C_6H_5S-	83-84	64.5	7.7		64.1	8.0	
$(CH_3)_3C$-	$H_3COC(O)CH_2S$-		49.3	7.7	6.4	49.4	7.7	6.2
$(CH_3)_3C$-	CH_3O-	(1.4460/24)	57.9	10.4	9.7	57.6	10.1	9.9
$(CH_3)_3C$-	CH_3CH_2O	(1.4420/24)			8.8			8.6
$(CH_3)_3C$-	C_6H_5O-	104-105			6.8			6.9
$(CH_3)_3C$-	NO_2-	124-125	45.0	7.6		45.2	7.8	
$CH_3S(CH_3)_2C$-[c]	H-	75-76						
$(CH_3)_3C$-	CH_3SCH_2-	84			8.0			8.1
$(CH_3)_3CC(=NOH)CH(SCH_3)CH_3$		128-129			8.0			7.8
$(CH_3)_3CC(=NOH)CH(CH_2)S$		117			6.8			7.2
$(CH_3)_3C$-	Cl-	102-103	48.2	8.1	9.4	48.3	8.1	9.5
$(CH_3)_3C$-[d]	Br-	111-112			7.2			7.1

[a] Single isomer. [b] Isomer mixture. [c] Payne et al. (1966). [d] Ramasseul and Rassat (1970).

19 g (0.4 mol) of methanethiol over 10 min at 0 ± 2 °C. To this solution of sodium thiomethoxide was added, dropwise, over 25 min, 50 g (0.28 mol) of 1-bromo-3,3-dimethyl-2-butanone. The temperature was maintained at 0 ± 3 °C during the addition and for an additional 30 min. The reaction mixture was filtered and the solvent removed by vacuum distillation. Fractional distillation of the residue gave the product as a colorless liquid, bp 73 °C (9.3 mm) (Asinger et al., 1958, report bp 73 °C (13 mm)).

3,3-Dimethyl-1-(methylthio)-2-butanone Oxime. A solution of 20.4 g (0.14 mol) of 1-methylthio-3,3-dimethyl-2-butanone, 19.6 g (0.28 mol) of hydroxylamine hydrochloride, and 14.8 g (0.14 mol) of sodium carbonate in 180 mL of 75% (v/v) aqueous ethanol was heated at reflux for 16 h. The two-phase residue after removal of the alcohol was taken up in ethyl acetate. Stripping of the dried organic solution yielded 21 g of residue which was distilled to give colorless liquid, bp 84 °C (0.5 mmHg), n^{24}_D 1.5011. The NMR spectrum contains signals at 1.21 [$(CH_3)_3C$-], 2.23 (-SCH_3), and 3.42 ppm (-CH_2-).

3,3-Dimethyl-1-(methylthio)-2-butanone O-[(Methylamino)carbonyl]oxime. Carbamate Method A. A solution of 110 g (0.68 mol) of 3,3-dimethyl-1-methylthio-2-butanone oxime, 142.8 g (0.75 mol) of methyl isocyanate, and three drops of triethylamine in 400 mL of anhydrous acetone was heated at reflux for 16 h. Volatiles were removed by stripping on a rotary evaporator to give 155 g of white solid residue, mp 50–53 °C. This was recrystallized by partial evaporation of a methylene chloride–hexane solution to yield white microcrystals, mp 57–58 °C. The NMR spectrum contains signals at 1.23 [$(CH_3)_3C$-], 2.22 (-SCH_3), 2.85 and 2.93 (-NCH_3), and 3.43 ppm (-CH_2-).

1-Bromo-3,3-dimethyl-2-butanone Oxime. A solution of 69.5 g (1.0 mol) of hydroxylamine hydrochloride in 100 mL of water was chilled in an ice bath as 90 g (0.5 mol) of 1-bromo-3,3-dimethyl-2-butanone was added. After addition of 100 mL of 95% ethanol, the mixture was stirred for 16 h and allowed to warm to room temperature. The resulting white slurry was filtered, and the solid was washed with water and dried to give 55 g of the desired compound, mp 111–112 °C (cf. Ramasseul and Rassat, 1970).

1-Azido-3,3-dimethyl-2-butanone O-[(Methylamino)carbonyl]oxime. Carbamate Method B. A slurry of 3.3 g (0.05 mol) of sodium azide and 10.0 g of 1-bromo-3,3-dimethyl-2-butanone O-[(methylamino)carbonyl]oxime in 50 mL of absolute ethanol was stirred at room temperature for 16 h, then filtered from solid. Addition of the filtrate to ice water yielded 8.6 g of solid which was recrystallized from hexane to give white crystals, mp 67–68 °C. The infrared spectrum contained a strong band at 4.83 μ.

3,3-Dimethyl-1-(methylthio)-2-butanone O-(Aminocarbonyl)oxime. Carbamate Method C. To a chilled solution of 5.4 g (0.055 mol) of phosgene in 50 mL of anhydrous ethyl ether was added, dropwise, 6.1 g (0.05 mol) of *N,N*-dimethylaniline, followed by a solution of 8.1 g (0.05 mol) of 3,3-dimethyl-1-(methylthio)-2-butanone oxime in 50 mL of ether. The mixture was stirred for 2 h, as it was allowed to come to room temperature, and then filtered. The chilled filtrate was treated over 15 min with 10 mL (0.15 mol) of 29% aqueous ammonia. After being stirred for an additional 15 min, the organic layer was separated, washed with water, and dried. Stripping of

solvent from the dried organic layer gave 10.1 g of a clear liquid residue which solidified on standing to an off-white solid, mp 58–60 °C.

3,3-Dimethyl-1-(methylthio)-2-butanone Oxime. Mixed Syn–Anti Isomers. Methanethiol (15.9 g, 0.33 mol) was added to a cold (–7 to 0 °C) solution of 6.9 g (0.3 g-atom) of sodium in 300 mL of anhydrous ethanol. After being stirred in the cooling bath for 0.5 h, the mixture was treated with 58.2 g (0.3 mol) of 1-bromo-3,3-dimethyl-2-butanone oxime over 10 min as the temperature was allowed to rise to over 35 °C. The resulting slurry was heated at 50 °C for 0.5 h, cooled, and filtered. The filtrate was stripped and the residue was taken up in benzene, filtered again, and restripped to give 51 g of liquid, n^{24}_D 1.5000. Distillation gave 42.3 g of colorless liquid, bp 79 °C (0.4 mm), n^{24}_D 1.5025. The NMR spectrum contains signals at 1.21 and 1.36 [$(CH_3)_3C$-], 2.07 and 2.23 (-SCH_3), and at 3.23 and 3.42 ppm (-CH_2-).

3,3-Dimethyl-1-(methylthio)-2-butanone O-[(Methylamino)carbonyl]oxime. Mixed Syn–Anti Isomers. A solution of 6.5 g (0.04 mol) of the oxime above, 2.4 g (0.042 mol) of methyl isocyanate, three drops of Et_3N, and 50 mL of benzene was heated under reflux for 16 h, cooled, and stripped on the rotary evaporator, finally at 2 mm and 50 °C, to give 9.4 g of viscous, pale-yellow liquid whose infrared spectrum was consistent with the proposed structure. The spectrum showed small differences as compared with the spectrum of the product of carbamate route A. The NMR spectrum contains signals at 1.23 and 1.35 [$(CH_3)_3C$-], 2.07 and 2.22 (-SCH_3), 2.85 and 2.93 (-NCH_3), and at 3.28 and 3.43 ppm (-CH_2-). The relative intensities of the NMR signals indicate an approximately equal mixture of isomers.

3,3-Dimethyl-1-(methylsulfinyl)-2-butanone O-[(Methylamino)carbonyl]oxime. A stirred slurry of 9.0 g (0.042 m) of sodium metaperiodate in 60 mL of water and 25 mL of methanol was cooled to 0 °C as 8.7 g (0.04 m) of 3,3-dimethyl-1-(methylthio)-2-butanone *O*-[(methylamino)-carbonyl]oxime was added in portions. After being stirred overnight at 0–10 °C, the mixture was allowed to come to room temperature, then stripped of volatiles. The residue was taken up in ethyl acetate. Stripping of the dried organic solution yielded 9.0 g of viscous liquid which solidified on standing. This was recrystallized from chloroform–hexane to give white solid, mp 78–79 °C.

3,3-Dimethyl-1-(methylsulfonyl)-2-butanone O-[(Methylamino)carbonyl]oxime. A solution of 54.5 g (0.25 m) of 3,3-dimethyl-1-(methylthio)-2-butanone *O*-[(methylamino)carbonyl]oxime in 250 mL of ethyl acetate was treated over 30 min with 105 g (0.55 m) of 40% peracetic acid. The temperature was held at 0–20 °C during the first half of the addition and at 20–35 °C during the second half by external cooling. After the exotherm had ceased (around 1 h), the solution was poured onto 1250 mL of hexane. The lower liquid layer was separated, taken up in 250 mL of chloroform, and washed to neutrality with saturated aqueous sodium bicarbonate. Stripping of the dried organic solution yielded 53 g of white solid which was recrystallized from chloroform–hexane to give white solid, mp 69–70 °C.

Biological Testing. The formulation used for the primary insecticide screens contains 500 ppm of test chemical, 4% acetone, 100 ppm Triton X-155, and water to total 100%. When lower concentrations are used in advanced testing, the solvent and surfactant concentrations are maintained.

The specific tests are briefly described below.

Mexican Bean Beetle and Southern Armyworm Tests. Paired, fully expanded primary leaves from Scarlet Runner bean plants are sprayed with the test formulation. After the spray deposit on the leaves is dry, the paired leaves are separated and each leaf is placed onto 1.5% water agar in separate petri dishes. One of the leaves is infested with ten 1-day old larvae of the Mexican bean beetle; the other with ten 2-day old larvae of the Southern armyworm. The covered dishes are held at 22 °C for 4 days after which mortality is determined.

Housefly Test. Stainless steel mesh cages containing ten adult houseflies are sprayed with the test formulation. The flies are supplied a sucrose solution by means of a paper wick for 3 days, after which mortality is determined.

Two-Spotted Spider Mite Spray and Systemic Tests. The primary leaves of lima bean plants (variety Sieva) are infested with mites 18–24 h before testing. To determine root uptake systemic activity, the soil in which the plants are growing is drenched with varying concentrations of test compound in the above formulation. Dosages are expressed as pounds/acre (on an area basis), with a maximum of 16. Contact activity is determined by spraying the previously infested plants with decreasing concentrations (parts per million) of chemicals. After 3 days, mortality is determined with the aid of a stereomicroscope.

Bean Aphid Spray and Systemic Tests. The test procedure followed is that described for the mites except the host plant is nasturtium (variety Dwarf Single).

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