

Synthesis and Miticidal and Insecticidal Activities of Biphenylhydrazinecarboxylates

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Ten biphenylhydrazinecarboxylates were obtained by the condensation of *o*-biphenylhydrazine with alkyl chloroformates. The miticidal and insecticidal activities of the new compounds were evaluated against *Tetranychus urticae* and *Sogatodes orizicola*. Structure-activity relationships for the screened compounds are discussed. Some of the compounds displayed greater activity than did the commercial standards, propargite and carbofuran.

INTRODUCTION

Phenylhydrazinecarboxylates have been investigated for their fungicidal (Frohberger et al., 1973; Werndl, 1973) and miticidal activity (Sato et al., 1987). The miticidal compounds reported by Sato et al. (1987) were substituted in the phenyl ring with alkyl or alkoxy groups. Dekeyser et al. (1991) found that an *o*-biphenyl substitution was important for miticidal activity in a series of 1,3,4-oxadiazinones. However, biphenyl compounds bearing the hydrazinecarboxylate grouping have not been studied. Therefore, as part of a continuing effort to develop new, highly efficacious pesticides, biphenylhydrazinecarboxylates (Figure 1) were synthesized to determine the effect of this type of substitution on miticidal and insecticidal activity. The compounds were tested against the two-spotted spider mite, *Tetranychus urticae*, and the rice delphacid, *Sogatodes orizicola*, which are two serious pests of agricultural crops.

Chemistry. Synthesis of the title compounds was achieved according to the method outlined in Scheme 1. The new biphenylhydrazinecarboxylates (IIa-j) were prepared by the condensation of *o*-biphenylhydrazine (I) with various alkyl chloroformates. The structural determination of the synthesized compounds was based on IR and ¹H NMR spectra (Table 1). The IR spectra of biphenylhydrazinecarboxylates IIa-j revealed a strong band around 1700 cm⁻¹ (ν_{C=O}) which is consistent with that found in other hydrazinecarboxylates (Hegarty and Tuohey, 1980; Garlaschelli and Gozzo, 1988). Yields of biphenylhydrazinecarboxylates IIa-j were in the range 69-80%.

Biology. Data on the miticidal and insecticidal activities of compounds IIa-j are presented in Table 2. The activity of biphenylhydrazinecarboxylates against mites was assessed by spraying cowpea plants with a solution of each compound, dissolved in a minimum volume of acetone and diluted with water containing a wetting agent, and 1 day later placing about 25 adult female mites on a treated cowpea leaf within a circle of tree tanglefoot. Five days later the plants were examined for live mites remaining on the leaves. Controls were treated identically except for the exclusion of test compound from the spray. The percentage mortality was estimated relative to the number of mites surviving on the control plants according to

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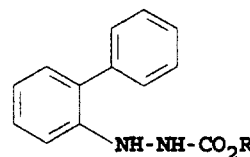


Figure 1. General structure of biphenylhydrazinecarboxylates.

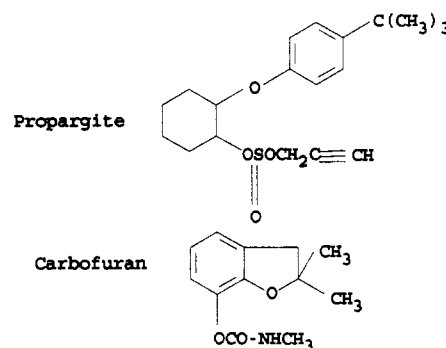
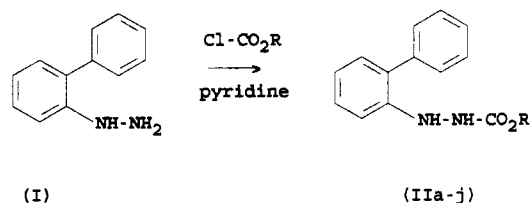


Figure 2. Structures of the commercial standards.

Scheme 1. Synthesis of Biphenylhydrazinecarboxylates



- IIa: R=CH₃
- IIb: R=C₂H₅
- IIc: R=CH₂C₆H₅
- IId: R=CH(CH₃)₂
- IIe: R=C₃H₇
- IIf: R=C₄H₉
- IIg: R=C₅H₁₁
- IIh: R=CH₂CH=CH₂
- III: R=C(CH₃)₃
- IIj: R=CH(CH₃)C₂H₅

Abbott's formula (Abbott, 1925). One replicate of each compound was tested at a concentration of 1000 ppm. The compounds yielding at least 90% mortality were further tested at 100 and 25 ppm. In these subsequent studies, four replicates were used at each concentration. A commercial miticide, propargite (Figure 2), was tested

Table 1. Yields, Melting Points, and Spectral Data of Compounds IIa-j

compd	yield	mp, °C	IR, $\nu_{C=O}$, cm^{-1}	$^1\text{H NMR}$ (CDCl_3), ppm
IIa	70	97-100	1700	6.8-7.5 (m, 11H), 3.5 (s, 3H)
IIb	73	92-95	1702	6.7-7.5 (m, 11H), 4.0 (q, 2H), 1.1 (t, 3H)
IIc	69	101-104	1720	6.8-7.5 (m, 16H), 5.1 (s, 2H)
IId	75	104-106	1699	6.9-7.5 (m, 11H), 4.8 (m, 1H), 1.1 (d, 6H)
IIe	76	88-90	1725	6.8-7.5 (m, 11H), 4.0 (t, 2H), 1.5 (m, 2H), 0.9 (t, 3H)
IIf	80	oil	1728	6.8-7.5 (m, 11H), 4.0 (t, 2H), 1.5 (m, 4H), 0.9 (t, 3H)
IIg	74	oil	1700	6.7-7.5 (m, 11H), 4.1 (t, 2H), 0.9-1.7 (m, 9H)
IIh	72	78-80	1701	6.8-7.5 (m, 11H), 5.0-5.9 (m, 3H), 4.5 (d, 2H)
IIi	70	92-94	1705	6.5-7.5 (m, 11H), 1.4 (s, 9H)
IIj	72	80-83	1700	6.8-7.5 (m, 11H), 4.7 (m, 1H), 1.4 (m, 2H), 1.1 (d, 3H), 0.9 (t, 3H)

for comparative purposes at two concentrations using four replicates per concentration.

The activity of biphenylhydrazinecarboxylates against rice delphacids was determined by spraying a pot containing about 20 rice seedlings at the two-leaf stage to runoff with a solution of each compound, prepared as in the mite study. One day after treatment, each pot was covered with a tubular cage and about 20 delphacids were transferred into each cage. Five days later, counts of the surviving delphacids in each cage were made, and percentage mortality was estimated with Abbott's formula. One replicate of each compound was tested at a concentration of 1000 ppm. Compounds yielding at least 90% mortality were tested further at 100 and 25 ppm. In the subsequent studies, 10 delphacids were transferred into each cage and two replicates were used at each concentration. A commercial insecticide, carbofuran (Figure 2), was tested for comparative purposes under the same conditions as the biphenylhydrazinecarboxylates.

EXPERIMENTAL PROCEDURES

Melting points were determined in open glass capillaries and are uncorrected. IR spectra in KBr were recorded on a Perkin-Elmer 283B spectrophotometer. $^1\text{H NMR}$ spectra were recorded on a Varian EM-360L (60 MHz) NMR spectrometer in CDCl_3 using TMS as internal reference; chemical shifts are expressed in parts per million.

***o*-Biphenylhydrazine (I).** Diazotization of *o*-aminobiphenyl as reported by Graebe and Rateanu (1894) furnished *o*-biphenylhydrazine in good yield. *o*-Aminobiphenyl was diazotized in concentrated HCl at 0 °C with sodium nitrite followed by reduction of the diazonium salt with stannous chloride. After filtration, the precipitate was recrystallized from water and then neutralized by sodium hydroxide, leaving the free base form of the hydrazine. A yield of 75% was obtained. The structure was confirmed by spectral analyses.

Biphenylhydrazinecarboxylates (IIa-j). A solution of appropriate alkyl chloroformate (0.01 mol) in toluene (10 mL) was added dropwise to a stirring, ice-cooled mixture of I (0.01 mol) and pyridine (0.01 mol) in toluene (100 mL). The reaction mixture was stirred for 2 h at room temperature and then poured into water (100 mL). The organic phase was separated, washed once with water (100 mL), dried over sodium sulfate, and then evaporated, leaving the desired product. Solid compounds were purified by recrystallization from a hexane/toluene mixture. Yields, melting points, and spectral data of biphenylhydrazinecarboxylates IIa-j are recorded in Table 1.

RESULTS AND DISCUSSION

The preparation of biphenylhydrazinecarboxylates IIa-j was a straightforward, high-yielding reaction between *o*-biphenylhydrazine (I) and alkyl chloroformates. Ten compounds, ranging from one to seven carbon atoms in the ester group, were prepared.

The mortality data in Table 2 indicate that all 10 biphenylhydrazinecarboxylates (IIa-j) showed excellent activity at 1000 ppm against two-spotted spider mites and rice delphacids, but in many cases the activity decreased sharply at lower concentrations.

Table 2. Miticidal and Insecticidal Screening Results of Compounds IIa-j

compd	% mortality <i>in vivo</i> at 5 days against					
	<i>T. urticae</i>			<i>S. orizicola</i>		
	1000 ppm	100 ppm	25 ppm	1000 ppm	100 ppm	25 ppm
IIa	100	24 (± 5) ^a	19 (± 4)	100	0 (± 0) ^b	0 (± 0)
IIb	100	25 (± 4)	30 (± 5)	100	27 (± 5)	21 (± 0)
IIc	100	11 (± 4)	17 (± 4)	100	3 (± 3)	3 (± 3)
IId	100	83 (± 7)	42 (± 6)	100	100 (± 0)	24 (± 0)
IIe	100	97 (± 3)	80 (± 10)	100	10 (± 0)	3 (± 3)
IIf	100	96 (± 4)	65 (± 9)	100	15 (± 4)	0 (± 0)
IIg	100	13 (± 4)	22 (± 5)	100	20 (± 0)	20 (± 0)
IIh	100	54 (± 7)	49 (± 7)	100	3 (± 3)	3 (± 3)
IIi	100	96 (± 3)	68 (± 7)	100	100 (± 0)	89 (± 0)
IIj	100	100 (± 0)	72 (± 9)	100	82 (± 5)	61 (± 5)
propargite	nd ^c	92 (± 7)	27 (± 5)	nd	nd	nd
carbofuran	nd	nd	nd	nd	100 (± 0)	53 (± 0)

^a Mean and standard error of four experiments. ^b Mean and standard error of two experiments. ^c nd, not determined.

The five most active miticidal compounds (IId-f,i,j) were found with a branched- or straight-chain length of three or four carbon atoms in the ester group. Some of these, for example the propyl ester (IIe), were clearly superior to the commercial miticide, propargite, at 25 ppm, the lowest concentration tested.

The three most active rice delphacid insecticides (IId,i,j) also possessed three or four carbon atoms in the ester group. Some of these, for example, the *tert*-butyl ester (IIi), were clearly superior to the commercial insecticide, carbofuran, at 25 ppm, the lowest concentration tested.

The results indicate that the presence of a branched alkyl group of three or four carbon atoms in the ester portion of biphenylhydrazinecarboxylates (IId,i,j) is important for potent activity against both mites and delphacids. Sato et al. (1987) also found potent miticidal properties with a branched-chain alkyl group in alkyl hydrazinecarboxylates; they report that isopropyl 2-methoxy-4-methyl-5-isopropylphenylhydrazinecarboxylate gave 95% control of *T. urticae* at a concentration of 200 ppm but its activity dropped to below 50% at 100 ppm (in-house data). In comparison, isopropyl biphenylhydrazinecarboxylate (IId) gave 83% at 100 ppm, which indicates that the biphenyl substitution enhances miticidal activity over alkyl- and alkoxyphenyl substitution. Another advantage to the biphenylhydrazine derivatives is the accompanying potent insecticidal activity, which appears to be absent from the compounds reported by Sato et al. (1987).

In conclusion, biphenylhydrazinecarboxylates displayed strong miticidal and rice delphacid activity and should be explored further. Future studies will examine the miticidal and insecticidal activity of *o*-biphenyldiazene carboxylates to determine whether these modifications enhance the pesticidal properties of this class of compounds over those of *o*-biphenylhydrazinecarboxylates.

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Received for review September 3, 1993. Revised manuscript received December 23, 1993. Accepted March 25, 1994.*

* Abstract published in *Advance ACS Abstracts*, May 1, 1994.