Synthesis and Miticidal Activity of *o*-Biphenyldiazenecarboxylates

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Nine *o*-biphenyldiazenecarboxylates were obtained in excellent yields by the air oxidation of *o*-biphenylhydrazinecarboxylates, catalyzed by palladium on charcoal. The miticidal activity of the new compounds was evaluated against *Tetranychus urticae*. Structure–activity relationships for the screened compounds are discussed. Some of the compounds displayed greater activity than did the commercial miticide propargite.

Keywords: *Miticides; o-biphenyldiazenecarboxylates; Tetranychus urticae*

INTRODUCTION

Phytophagous mites are serious pests on many important agricultural crops. The market for miticides is currently about $500 million U.S. (Dekeyser and Downer, 1994). There is a continuing search for new, specific miticides as existing ones become less effective through the development of resistance or are removed from the market due to toxicology issues. We have identified 1,3,4-oxadiazinones as novel miticides (Dekeyser et al., 1988). Our studies have shown that an *o*-biphenyl substitution was important for miticidal activity in these compounds (Dekeyser et al., 1991). Recently, we have also found that *o*-biphenyl substitution in a series of hydrazinecarboxylates produced strong miticidal properties and insecticidal activity against rice delphacids (Dekeyser et al., 1994). A further modification would be to introduce a double bond into the hydrazinecarboxylate portion of these compounds, thus forming diazenecarboxylates, as in Figure 1.

Aryldiazenecarboxylates (Ar–N=N–CO_2R) have been investigated for their photographic, fungicidal, and antifeeding properties (Compere et al., 1979; Weinman et al., 1970; Galun et al., 1969). Benzofuranyl- and benzopyranyldiazenecarboxylates appear to be the only reported diazenecarboxylates that show miticidal properties (Pilgram and Skiles, 1985a,b). Therefore, as part of a continuing effort to develop new, highly efficacious miticides, *o*-biphenyldiazenecarboxylates (Figure 1) were synthesized to determine whether this type of substitution enhances the miticidal activity found with *o*-biphenylhydrazinecarboxylates. The compounds were tested against a very important mite pest, the two-spotted spider mite, *Tetranychus urticae*, and their activities were compared with that of a major commercial miticide, propargite (Figure 2).

Chemistry. Synthesis of the title compounds was achieved according to the method outlined in Scheme 1. The *o*-biphenylhydrazinecarboxylates **Ia–Ii** were prepared by the condensation of *o*-biphenylhydrazine with various alkyl chloroformates, as described by Dekeyser et al. (1994). The title compounds **IIa–IIi** were obtained by the oxidation of **Ia–Ii** using a modification of the method of Gaviraghi et al. (1981). The

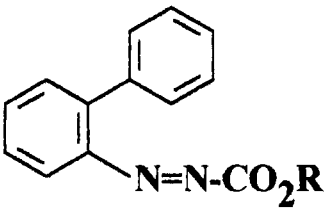


Figure 1. General structure of *o*-biphenyldiazenecarboxylates.

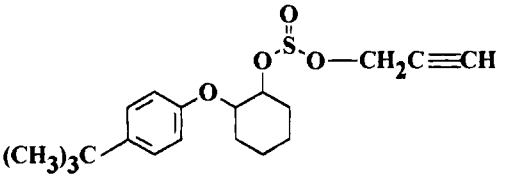
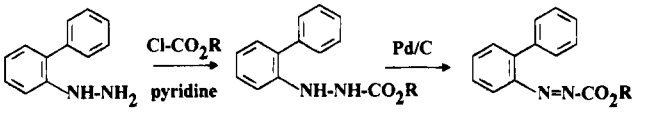


Figure 2. Structure of the commercial miticide propargite.

Scheme 1. Synthesis of *o*-Biphenyldiazenecarboxylates



R
Ia, IIa: CH_3
Ib, IIb: C_2H_5
Ic, IIc: c-C_5H_9
Id, IId: $CH(CH_3)_2$
Ie, IIe: C_3H_7
If, IIf: $C(CH_3)_3$
Ig, IIg: $CH(CH_3)C_2H_5$
Ih, IIh: $CH_2CH{=}CH_2$
Ii, IIi: $CH{=}CH_2$

structural determination of the synthesized compounds was based on IR and ^{1}H NMR spectra (Table 1). The IR spectra of *o*-biphenyldiazenecarboxylates **IIa–IIi** revealed a strong band at about 1750 cm^{-1} ($\nu_{C=O}$), which is consistent with that found in diazenecarboxylates reported by Gaviraghi et al. (1981). Yields of *o*-biphenyldiazenecarboxylates **IIa–IIi** were in the range 85–96%.

Biology. Data on the miticidal activity of compounds **IIa–IIi** are presented in Table 2. The activity of *o*-biphenyldiazenecarboxylates against mites was as-

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Table 1. Yield and Spectral Data of Compounds IIa–IIi

compd	% yield	IR, $\nu_{C=O}$, cm^{-1}	^1H NMR ($CDCl_3$), ppm
IIa	85	1758	7.3–7.7 (m, 9H), 4.0 (s, 3H)
IIb	88	1746	7.4–7.7 (m, 9H), 4.5 (q, 2H), 1.5 (5, 3H)
IIc	87	1750	7.2–7.6 (m, 9H), 5.2 (m, 1H), 1.6–2.0 (m, 8H)
IId	90	1755	7.3–7.8 (m, 9H), 5.1 (m, 1H), 1.3 (d, 6H)
IIe	96	1755	7.3–7.7 (m, 9H), 4.2 (t, 2H), 1.5 (m, 2H), 0.9 (t, 3H)
IIf	92	1758	7.4–7.8 (m, 9H), 1.5 (s, 9H)
IIg	94	1750	7.4–7.8 (m, 9H), 5.0 (m, 1H), 1.5 (m, 2H), 1.2 (d, 3H), 1.0 (t, 3H)
IIh	90	1753	7.3–7.8 (m, 9H), 5.0–5.9 (m, 3H), 4.8 (d, 2H)
IIi	90	1764	7.3–7.7 (m, 9H), 4.4–5.1 (m, 3H)

Table 2. Miticidal Screening Results of Compounds IIa–IIi

	% mortality *in vivo* at 5 days against *T. urticae*		
compd	1000 ppm	100 ppm	25 ppm
IIa	50	nd[a]	nd
IIb	98	10 (±4)[b]	0 (±0)
IIc	100	100 (±0)	38 (±7)
IId	70	nd	nd
IIe	70	nd	nd
IIf	100	74 (±9)	54 (±7)
IIg	100	85 (±7)	79 (±5)
IIh	100	96 (±4)	8 (±4)
IIi	95	41 (±5)	34 (±2)
propargite	nd	96 (±4)	24 (±5)

[a] nd, not determined. [b] Mean and standard error of four experiments.

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

EXPERIMENTAL PROCEDURES

IR spectra were recorded on a Perkin-Elmer 283B spectrophotometer. ^1H 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.** 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.

***o*-Biphenylhydrazinecarboxylates (Ia–Ii).** An appropriate alkyl chloroformate was added to *o*-aminobiphenyl and pyridine according to the method of Dekeyser et al. (1994). The reaction afforded *o*-biphenylhydrazinecarboxylates (**Ia–Ii**) in good yields. Solid compounds were purified by recrystallization from a hexane/toluene mixture. The structures were confirmed by spectral analyses.

***o*-Biphenyldiazenecarboxylates (IIa–IIi).** A solution of **I** (0.01 mol) in toluene (50 mL) was treated with activated 10% palladium on charcoal (1 g) at room temperature and allowed to stir until completion of the reaction, as determined by TLC (generally about 4 h). The TLC solvent mixture was dichloromethane. Then, the reaction mixture was filtered and the solvent evaporated, leaving a reddish oil which was essentially pure by IR and NMR spectral analyses. Yields and spectral data of *o*-biphenyldiazenecarboxylates **IIa–IIi** are recorded in Table 1.

RESULTS AND DISCUSSION

The preparation of *o*-biphenyldiazenecarboxylates **IIa–IIi** was accomplished by the oxidation of the corresponding *o*-biphenylhydrazinecarboxylates in high yields (85–96%) using very mild conditions. It was found that the use of magnetic stirring in an open vessel was sufficient for the reaction to occur, whereas the use of an aspirator to bubble air into the reaction mixture was recommended by Gaviraghi et al. (1981). Nine compounds, ranging from one to five carbon atoms in the ester group, were prepared.

The mortality data in Table 2 indicate that all nine *o*-biphenyldiazenecarboxylates **IIa–IIi** were toxic to two-spotted spider mites at 1000 ppm, but in many cases the activity decreased sharply at lower concentrations. The four most active miticidal compounds (**IIc, IIf, IIg, IIi**) were found with a saturated branched chain of four or five carbon atoms or an unsaturated chain of two carbon atoms in the ester group. Some of these, for example the *sec*-butyl ester (**IIg**), were clearly superior to the commercial miticide, propargite, at 25 ppm, the lowest concentration tested.

The results indicate that the presence of a branched alkyl group of four carbon atoms in the ester portion of *o*-biphenyldiazenecarboxylates (**IIf, IIg**) is optimal for potent activity against mites. The corresponding *o*-biphenylhydrazinecarboxylates showed similar miticidal activity, which indicates that the diazene derivatives do not present an advantage over the analogous hydrazine compounds. Furthermore, in contrast to their hydrazinecarboxylate counterparts, the diazenecarboxylates did not possess appreciable insecticidal activity (P. T. McDonald, personal communication).

Overall, the findings from this study suggest that *o*-biphenyldiazenecarboxylates are a new class of highly specific and potent miticides.

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