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Synthesis and Insecticidal Evaluation of Novel *N*-Oxalyl Derivatives of Tebufenozide

CHUN HUI MAO,[†,§] QING MIN WANG,*[,†] RUN QIU HUANG,[†] FU CHUN BI,[†] LI CHEN,[†] YU XIU LIU,[†] AND JIAN SHANG[†]

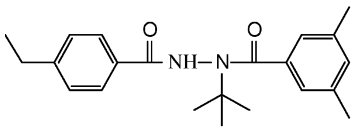
Research Institute of Elemento-Organic Chemistry, State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, People's Republic of China, and Hunan Branch of National Pesticide Research and Development South Center, Changsha 410007, People's Republic of China

A series of novel *N′-tert*-butyl-*N′*-3,5-dimethylbenzoyl-*N*-aryloxyoxalyl-*N*-4-ethylbenzoyl hydrazines containing a carboxylic acid or ester substituent on the aryl were synthesized, and their larvicidal activities were evaluated. The results of bioassays indicated that some of these title compounds exhibit higher larvicidal activities than RH5849 (*N-tert*-butyl-*N*,*N′*-dibenzoylhydrazine), but they are not good compared to the parent compound (tebufenozide). The carboxylic acid substituent on the aryl was essential for high larvicidal activity. Compared to the parent compound, these derivatives displayed different physical properties, for example, better solubility in organic solvents. Toxicity assays indicated that these derivatives could induce a premature, abnormal, and lethal larval molt.

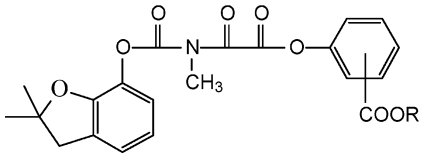
KEYWORDS: ***N*-Oxalyl derivative; tebufenozide; RH-5992; RH-5849; diacylhydrazine; larvicidal activity; lethal larval molt; ecdysone**

INTRODUCTION

Recently, synthetic substituted *N′-tert*-butyl-*N*,*N′*-diacylhydrazines have been found to work as nonsteroidal ecdysone agonists inducing, especially in *Lepidoptera*, precocious molting, leading to death (*1*−*5*). One of these, *N-tert*-butyl-*N′*-4-ethylbenzoyl)-*N*-3,5-dimethylbenzoylhydrazide (tebufenozide; RH-5992) (**A**), was the first to be commercialized as a



A



B

leptidopteran-specific insecticide under the trade names Mimic, Confirm, and Romdan in several countries (*6*, *7*). However, tebufenozide does not have systemic action and has low solubility in water and limited solubility in common organic solvents, and these disadvantages impede its field application (*8*, *9*).

The activity spectrum of a pesticidal compound is often determined by the physical properties of the compound, and it is possible to convert a nonsystemic compound into one that is systemic by attaching an appropriate functional group to an insecticide. Moreover, the physical properties of an insecticidal compound may be manipulated to obtain products with other selected types of activity by proper selection of the derivatizing moiety (*10*). In our previous work, the synthesis and insecticidal evaluation of a series of novel N-sulfenylated derivatives of diacylhydrazines have been reported, and the results of bioassay showed that they exhibit excellent larvicidal activity, inducing a premature, abnormal and lethal molting, and have better solubility than the parent diacylhydrazines at the same time (*9*, *11*, *12*). Recently it was reported that *N*-oxalyl derivatives of carbofuran containing a carboxylic acid or ester substituent (**B**) displayed a wide spectrum of systemic pesticide activity comparable or superior to that of carbofuran in the cut stem, soil, and foliar applications. It was believed that the derivatives containing a carboxylate moiety may result in compounds that possibly have unusual systemic activity because carboxylic acid groups are phloem mobile and may move downward as well as upward in plants (*13*). Encouraged by these reports, we developed an idea for the introduction of an aryloxy-oxalyl containing a carboxylic acid or ester substituent into *N-tert*-butyl-*N′*-4-ethylbenzoyl-*N*-3,5-dimethyl benzoylhydrazide (tebufenozide). Therefore, in a search for new insect growth regulators with improved profiles, we designed and synthesized

* Author to whom correspondence should be addressed [telephone +86-(0)22-23504229; fax +86-(0)22-23503438; e-mail wang98h@263.net].
† State Key Laboratory of Elemento-Organic Chemistry.
§ Hunan Branch of National Pesticide Research and Development South Center.

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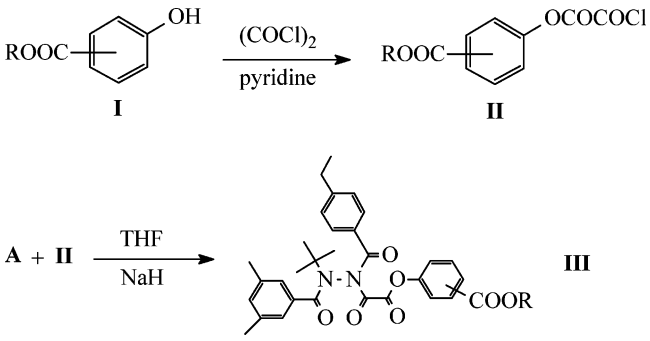
Scheme 1. General Synthetic Route for Compounds **III**



a series of novel *N*′-*tert*-butyl-*N*′-3,5-dimethylbenzoyl-*N*-aryloxyoxalyl-*N*-4-ethylbenzoyl hydrazines containing carboxylic acid or ester substituent derivatives on the aryl group (**III** and **IV**) as shown in **Schemes 1** and **2**.

MATERIALS AND METHODS

General Synthetic Procedure for Substituted Aryloxyoxalyl Chloride (II). To a mixture of hydroxybenzonate ester **(I)** (5.0 mmol) and 10 mL of dry dichloromethane was added oxalyl chloride (7.5 mmol) in one portion. The mixture was chilled in an ice−water bath, and pyridine (7.5 mmol) in 5 mL of dichloromethane was added dropwise with stirring. After the addition of pyridine, the mixture was stirred at room temperature for 30 min. Pyridine hydrochloride was removed by filtration, and the filtrate was concentrated under vacuum. Hexane (50 mL) was added to the residue, and the mixture was filtered again to remove residual pyridine hydrochloride; hexane was removed under vacuum to give substituted aryloxyoxalyl chloride **(II)** as a colorless oily liquid, which was used for further operations without purification.

General Synthetic Procedure for *N*′-*tert*-Butyl-*N*′-3,5-dimethylbenzoyl-*N*-aryloxyoxalyl-*N*-4-ethylbenzoyl Hydrazines (IIIa−l). To a stirred solution of *N*-*tert*-butyl-*N*′-4-ethylbenzoyl-*N*-3,5-dimethylbenzoylhydrazide **(A)** (5.0 mmol) in anhydrous tetrahydrofuran (50 mL) was added portionwise sodium hydride (0.24 g, 50% oil dispersion, 5.0 mmol) at room temperature under nitrogen. The mixture was stirred at room temperature for 1 h and cooled to 0 °C, and then the substituted aryloxyoxalyl chloride **(II)** (5.0 mmol) in anhydrous tetrahydrofuran (8 mL) was added dropwise. After the addition was complete, the reaction mixture was stirred for 5 h at room temperature. Then the solid was filtered off, and the filtrate was concentrated under vaccum. The residue was purified by column chromatography on a silica gel using 6:1 petroleum ether (60−90 °C)/ethyl acetate as the eluent to afford compounds **IIIa**−**l** as colorless crystallines.

General Synthetic Procedure for *N*′-*tert*-Butyl-*N*′-3,5-dimethylbenzoyl-*N*-aryloxyoxalyl-*N*-4-ethylbenzoyl Hydrazines (IVa−c). *N*′-*tert*-Butyl-*N*′-3,5-dimethylbenzoyl-*N*-benzyloxycarbonylaryloxyoxalyl-*N*-4-ethylbenzoyl hydrazines (**IIId**, **IIIh**, **IIIl**) (2.4 mmol) dissolved in ethyl acetate (20 mL) were added to a catalytic amount (0.30 g) of 5% palladium on carbon. The resulting mixture was stirred, and hydrogen gas was introduced over 1.5 h at room temperature. Then the reaction mixture was filtered to remove solids, and the organic filtrate was concentrated under reduced pressure to yield the compounds **IVa**−**c** as a white solid.

Biological Assay. The larvicidal activities of the novel *N*-oxalyl derivatives **(IIIa**−**l**, **IVa**−**c),** the parent compound (tebufenozide), and RH-5849 (*N*-*tert*-butyl-*N*,*N*′-dibenzoylhydrazine) were evaluated using a previously reported procedure (*8*, *9*, *11*, *12*). The larvicidal activity was tested against Oriental armyworm [*Mythimna* (= *Pseudaletia*) *separata* (Walker)] by foliar application. For the foliar armyworm tests, individual corn leaves were placed on moistened pieces of filter paper in Petri dishes. The leaves were then sprayed with the test solution and allowed to dry. The dishes were infested with 10 fourth-instar armyworm larvae. Percentage mortalities were evaluated 4 days after treatment. Each treatment was performed in triplicate. Evaluations are based on a percentage scale of 0−100 in which 0 equals no activity and 100 equals total kill. Error of the experiments was 5%. For comparative purposes, the parent compound (tebufenozide) was tested under the same conditions. The larvicidal activity is summarized in **Table 3**.

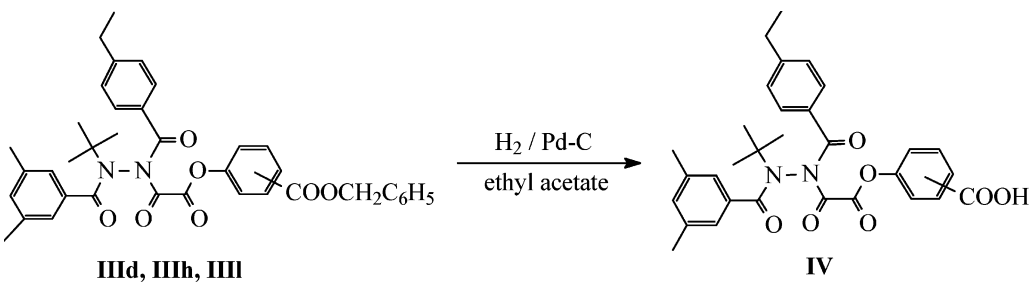
RESULTS AND DISCUSSION

Synthesis. *N*-*tert*-Butyl-*N*′-4-ethylbenzoyl-*N*-3,5-dimethylbenzoylhydrazide **(A)** was synthesized according to the reported procedure (*14*). Substituted aryloxyoxalyl chlorides **(II)** were prepared by the reaction of different hydroxybenzonate esters **(I)** with oxalyl chloride in dichloromethane using pyridine as the acid acceptor. Then the key intermediates were reacted with *N*-*tert*-butyl-*N*′-4-ethylbenzoyl-*N*-3,5-dimethylbenzoylhydrazide (**A**) in the dry THF using sodium hydride as alkali to yield *N*′-*tert*-butyl-*N*′-3,5-dimethylbenzoyl-*N*-aryloxyoxalyl-*N*-4-ethylbenzoyl hydrazines containing a carboxylate substituent **(III)** as shown in **Scheme 1**. The novel *N*-oxalyl derivatives of tebufenozide containing carboxylic acid substituents **(IV)** were synthesized by hydrogenation of the *N*′-*tert*-butyl-*N*′-3,5-dimethylbenzoyl-*N*-benzyloxylcarbonylaryloxyoxalyl-*N*- 4-ethylbenzoylhydrazines **(IIId**, **IIIh**, **IIIl)** in excellent yields using palladium on carbon as catalyst as shown in **Scheme 2**. The physical properties and elemental analyses of the new compounds **(IIIa**−**l**, **IVa**−**c)** are listed in **Table 1**, and their ^{1}H NMR data are listed in **Table 2**.

First, we attempted to react *N*-*tert*-butyl-*N*′-4-ethylbenzoyl-*N*-3,5-dimethylbenzoylhydrazide (**A**) with oxalyl chloride to yield the corresponding *N*-oxalyl chloride, which was further reacted with hydroxybenzonate esters **(I)** to yield the title compounds **III**. We obtained 2-(3,5-dimethyl)phenyl-5-(4-ethyl)-phenyl-1,3,4-oxadiazole instead of the *N*-oxalyl chloride of *N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines when compound **A** was treated with oxalyl chloride in dichloromethane using pyridine as the acid acceptor at room temperature. Under reflux in 1,2-dichloroethane without pyridine, the reaction yielded 2-(3,5-dimethyl)phenyl-5-(4-ethyl)-phenyl-1,3,4-oxadiazole and 4-*tert*-butyl-2-(4-ethylphenyl)-4*H*-1,3,4-oxadiazine-5,6-dione at the same time.

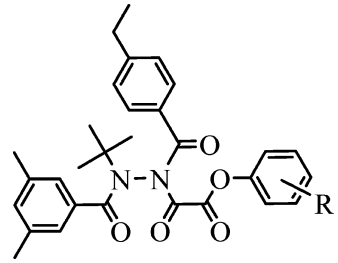
Insecticidal Activity. Table 3 shows the insecticidal activity of the parent compound (tebufenozide) and RH5849 (*N*-*tert*-

Scheme 2. General Synthetic Route for Compounds **IV**



IIId, IIIh, IIIl **IV**

Table 1. Physical Properties and Elemental Analyses of *N*-Oxalyl Derivatives of Tebufenozide (**IIIa**–**l**, **IVa**–**c**)



					analysis calcd (found, %)		
compd	R	mp (°C)	yield (%)	formula	C	H	N
IIIa	*p*-$COOCH_3$	141–142	41.2	$C_{32}H_{34}N_2O_7$	68.80 (69.00)	6.13 (6.09)	5.01 (5.17)
IIIb	*p*-$COOC_4H_9n$	106–108	41.0	$C_{35}H_{40}N_2O_7$	69.98 (69.77)	6.71 (6.90)	4.66 (4.63)
IIIc	*p*-$COOC_3H_7i$	144–146	51.3	$C_{34}H_{38}N_2O_7$	69.61 (69.64)	6.53 (6.59)	4.77 (4.65)
IIId	*p*-$COOCH_2C_6H_5$	127–128	42.6	$C_{38}H_{38}N_2O_7$	71.91 (71.90)	6.03 (6.05)	4.41 (4.53)
IIIe	*o*-$COOCH_3$	131–133	42.7	$C_{32}H_{34}N_2O_7$	68.80 (68.80)	6.13 (6.10)	5.01 (5.23)
IIIf	*o*-$COOC_4H_9n$	100–102	44.4	$C_{35}H_{40}N_2O_7$	69.98 (70.10)	6.71 (6.90)	4.66 (4.65)
IIIg	*o*-$COOC_3H_7i$	138–140	39.3	$C_{34}H_{38}N_2O_7$	69.61 (69.64)	6.53 (6.47)	4.77 (4.89)
IIIh	*o*-$COOCH_2C_6H_5$	128–130	42.0	$C_{38}H_{38}N_2O_7$	71.91 (71.79)	6.03 (6.00)	4.41 (4.48)
IIIi	*m*-$COOCH_3$	97–99	50.0	$C_{32}H_{34}N_2O_7$	68.80 (68.81)	6.13 (6.09)	5.01 (5.06)
IIIj	*m*- $COOC_4H_9n$	115–116	46.7	$C_{35}H_{40}N_2O_7$	69.98 (70.15)	6.71 (6.93)	4.66 (4.84)
IIIk	*m*- $COOC_3H_7i$	119–120	34.2	$C_{34}H_{38}N_2O_7$	69.61 (69.56)	6.53 (6.64)	4.77 (4.85)
IIIl	*m*-$COOCH_2C_6H_5$	112–114	32.0	$C_{38}H_{38}N_2O_7$	71.91 (71.80)	6.03 (6.06)	4.41 (4.33)
IVa	*p*-COOH	174–176	95.0	$C_{31}H_{32}N_2O_7$	68.37 (68.40)	5.92 (5.84)	5.14 (5.34)
IVb	*o*-COOH	158–159	94.1	$C_{31}H_{32}N_2O_7$	68.37 (68.21)	5.92 (5.86)	5.14 (5.19)
IVc	*m*-COOH	176–178	92.5	$C_{31}H_{32}N_2O_7$	68.37 (68.18)	5.92 (5.87)	5.14 (5.20)
BDPH	H	140–142	45	$C_{30}H_{32}N_2O_5$	71.98 (71.87)	6.44 (6.48)	5.60 (5.71)

Table 2. ^{1}H NMR Data of *N*-Oxalyl Derivatives of Tebufenozide

compd	^{1}H NMR (CD_3Cl), δ
IIIa	1.19 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.68 (s, 9H, $C(CH_3)_3$); 2.17 (s, 6H, Ph-$(CH_3)_2$); 2.63 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 3.89 (s, 3H, OCH_3); 6.44–7.90 (m, 11H, Ph)
IIIb	0.97 (t, $^3J_{HH}$ = 7.5 Hz, 3H, $O(CH_2)_3CH_3$); 1.19 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.39–1.51 (m, 4H, $O(CH_2C_2H_4CH_3$); 1.69 (s, 9H, $C(CH_3)_3$); 2.17 (s, 6H, Ph-$(CH_3)_2$); 2.63 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 4.30 (t, $^3J_{HH}$ = 6.6 Hz, 2H, O–CH_2); 6.44–7.90 (m, 11H, Ph)
IIIc	1.20 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.35 (d, $^3J_{HH}$ = 6.0 Hz, 6H, $CH(CH_3)_2$); 1.69 (s, 9H, $C(CH_3)_3$); 2.17 (s, 6H, Ph-$(CH_3)_2$); 2.64 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 5.16–5.26 (m, 1H, O–CH); 6.44–7.90 (m, 11H, Ph)
IIId	1.18 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.68 (s, 9H, $C(CH_3)_3$); 2.17 (s, 6H, Ph-$(CH_3)_2$); 2.62 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 5.33 (s, 2H, O–CH_2); 6.44–7.93 (m, 16H, Ph)
IIIe	1.26 (t, $^3J_{HH}$ = 7.8 Hz, 3H, Ph-CH_2CH_3); 1.70 (s, 9H, $C(CH_3)_3$); 2.15 (s, 6H, Ph-$(CH_3)_2$); 2.69 (q, $^3J_{HH}$ = 7.8 Hz, 2H, Ph-CH_2CH_3); 3.88 (s, 3 H, OCH_3); 5.84–7.93 (m, 11H, Ph)
IIIf	0.97 (t, $^3J_{HH}$ = 7.5 Hz, 3H, $O(CH_2)_3CH_3$); 1.25 (t, $^3J_{HH}$ = 7.8 Hz, 3H, Ph-CH_2CH_3); 1.35–1.47 (m, 4H, $OCH_2C_2H_4CH_3$); 1.70 (s, 9H, $C(CH_3)_3$); 2.14 (s, 6H, Ph-$(CH_3)_2$); 2.68 (q, $^3J_{HH}$ = 7.8 Hz, 2H, Ph-CH_2CH_3); 4.25–4.34 (m, 2H, O–CH_2); 5.84–7.93 (m, 11H, Ph)
IIIg	1.25 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.34 (dd, 6H, *J* = 6.0 Hz, $CH(CH_3)_2$); 1.70 (s, 9H, $C(CH_3)_3$); 2.14 (s, 6H, Ph-$(CH_3)_2$); 2.67 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 5.16–5.28 (m, 1H, O–CH); 5.75–7.92 (m, 11H, Ph)
IIIh	1.25 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.67 (s, 9H, $C(CH_3)_3$); 2.15 (s, 6H, Ph-$(CH_3)_2$); 2.68 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 5.34 (s, 2H, O–CH_2); 5.81–7.96 (m, 16H, Ph)
IIIi	1.17 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.69 (s, 9H, $C(CH_3)_3$); 2.17 (s, 6H, Ph-$(CH_3)_2$); 2.64 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 3.90 (s, 3H, OCH_3); 6.58–7.86 (m, 11H, Ph)
IIIj	0.90 (t, $^3J_{HH}$ = 6.9 Hz, 3H, $O(CH_2)_3CH_3$); 1.07 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.32–1.44 (m, 4H, $OCH_2C_2H_4CH_3$); 1.61 (s, 9H, $C(CH_3)_3$); 2.09 (s, 6H, Ph-$(CH_3)_2$); 2.55 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 4.22 (t, $^3J_{HH}$ = 6.0 Hz, 2H, O–CH_2); 6.40–7.77 (m, 11H, Ph)
IIIk	1.08 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.27 (d, $^3J_{HH}$ = 6.0 Hz, 6H, $CH(CH_3)_2$); 1.61 (s, 9H, $C(CH_3)_3$); 2.09 (s, 6H, Ph-$(CH_3)_2$); 2.55 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 5.10–5.18 (m, 1H, O–CH); 6.36–7.76 (m, 11H, Ph)
IIIl	1.12 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.69 (s, 9H, $C(CH_3)_3$); 2.16 (s, 6H, Ph-$(CH_3)_2$); 2.57 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 5.34 (s, 2H, O–CH_2); 6.53–7.90 (m, 16H, Ph)
IVa	1.19 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.70 (s, 9H, $C(CH_3)_3$); 2.17 (s, 6H, Ph-$(CH_3)_2$); 2.64 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 6.49–7.97 (m, 11H, Ph)
IVb	1.27 (t, $^3J_{HH}$ = 7.8 Hz, 3H, Ph-CH_2CH_3); 1.69 (s, 9H, $C(CH_3)_3$); 2.14(s, 6H, Ph-$(CH_3)_2$); 2.69 (q, $^3J_{HH}$ = 7.8 Hz, 2H, Ph-CH_2CH_3); 5.96–8.04 (m, 11H, Ph)
IVc	1.10 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Ph-CH_2CH_3); 1.61 (s, 9H, $C(CH_3)_3$); 2.09 (s, 6H, Ph-$(CH_3)_2$); 2.57 (q, $^3J_{HH}$ = 7.5 Hz, 2H, Ph-CH_2CH_3); 6.60–7.85 (m, 11H, Ph)
BDPH	1.20 (t, $^3J_{HH}$ = 7.5 Hz, 3H, Me), 1.70 (s, 9H, Bu^t), 2.17 (s, 6H, Me-Ph), 2.63 (q, $^3J_{HH}$ = 7.5 Hz, 2H, CH_2), 6.37–7.02 (m, 12H, Ph)

butyl-*N*,*N*′-dibenzoylhydrazine) and synthesized derivatives against Oriental armyworm [*Mythimna* (= *Pseudaletia*) *separata* (Walker)]. The results indicate that some of these title compounds exhibit higher larvicidal activities than RH5849 (*N*-*tert*-

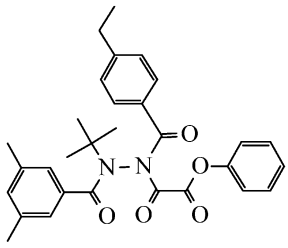
Table 3. Larvicidal Activities of *N*-Oxalyl Derivatives of Tebufenozide and Parent Compound, Tebufenozide

	larvicidal activity (%) at							
compd	500 mg kg^{-1}	100 mg kg^{-1}	50 mg kg^{-1}	30 mg kg^{-1}	25 mg kg^{-1}	10 mg kg^{-1}	5 mg kg^{-1}	LC_{50} (mg/L)
IIIa	100	100	100		85	55		9.79
IIIb	100	100	100		100	0		13.89
IIIc			100		90	20		16.33
IIId	100		100		70	10		18.11
IIIe	100	100	100		60	0		20.89
IIIf	100		75		40	0		30.76
IIIg	100	95	45		30	0		41.59
IIIh	100		85			10		27.80
IIIi			100		75	0		17.74
IIIj			100	95		15		15.85
IIIk			100	90		15		18.16
IIIl			100		42.5	0		18.75
IVa	100		100		100	95	45	4.82
IVb	100	0						336.51
IVc			100		100	73.3	55	5.16
tebufenozide						100	70	1.59
RH5849	100	100	95					24.38

butyl-*N*,*N*′-dibenzoylhydrazine), but they are not good compared to the parent compound (tebufenozide). For example, the most active compound, **IVa**, requires 3 times the concentration for the LC_{50} as does tebufenozide. Toxicity assays indicated that the title compounds, like the parent compound, can induce a premature, abnormal, and lethal larval molt. Symptoms of toxicity included discoloration, weight loss, cessation of feeding, and developmentally premature, lethal molting at higher rates.

It is interesting to note that the larvicidal activities of the title compounds appeared to be strongly associated with the substituent R and its position on the benzene. The derivatives with substituent R at the meta or para position are obviously superior to those with R at the ortho position. The derivatives containing carboxylic acid (**IVa** and **IVc**) are much better than those containing carboxylate ester, and those derivatives containing carboxylic acid on the meta or para (**IVa** and **IVc**) position are comparable to the patent compound tebufenozide. Compound **IVb** displayed reduced larvicidal activity, maybe because the H atom of carboxylic acid at the ortho of the benzene ring can provide an intramolecular hydrogen bond with the carbonyl of the oxalyl group, which alters the properties of the compound.

To explore further the effect of the carboxylic acid substituent on the aryl upon larvicidal activity, *N*′-*tert*-butyl-*N*′-3,5-dimethylbenzoyl-*N*-phenyloxyoxalyl-*N*-4-ethylbenzoyl hydrazine (BDPH) was synthesized using the same procedure as shown in **Scheme 1**.



BDPH

The larvicidal activity (LC_{50}) of BDPH was 17.50 mg/L. Hence, we conclude that the carboxylic acid substituent on the aryl was essential for high larvicidal activity.

There is difficulty in using previous *N*-*tert*-butyl-*N*,*N*′-dibenzoylhydrazine insecticides. They have very low solubity in water and limited solubility in common organic solvents, so application of such diacylhydrazines in water and as emulsifiable concentrates is not ordinarily feasible (*9*). Compared to the parent compound (tebufenozide), the title compounds displayed better solubility in organic solvents such as methylene dichloride, chloroform, toluene, and xylene, which should make them easier to apply under field conditions.

It was reported that for an insecticide to be phloem mobile, a −COOH functional group would be necessary (*15*); therefore, substitution of a carboxylate or carboxylic acid group to tebufenozide may help phloem movement of the compound. However, we found that the title compounds have no systemic activity.

Conclusions. In summary, a series of novel *N*′-*tert*-butyl-*N*′-3,5-dimethylbenzoyl-*N*-aryloxyoxalyl-*N*-4-ethylbenzoyl hydrazines contaning carboxylic acid or carboxylate substituent on the aryl were synthesized. The results of bioassays showed that some of these title compounds exhibit higher larvicidal activities than RH5849 (*N*-*tert*-butyl-*N*,*N*′-dibenzoylhydrazine), but they are not good compared to the parent compound (tebufenozide). The carboxylic acid substituent on the aryl was essential for high larvicidal activity. Compared to the parent compound, these derivatives displayed different physical properties, which may lead to compounds with better biological activity and characteristics.

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