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Synthesis and Insecticidal Activities of Novel *N*-Sulfenyl-*N′*-*tert*-butyl-*N,N′*-diacylhydrazines. 2. N-Substituted Phenoxysulfenate Derivatives

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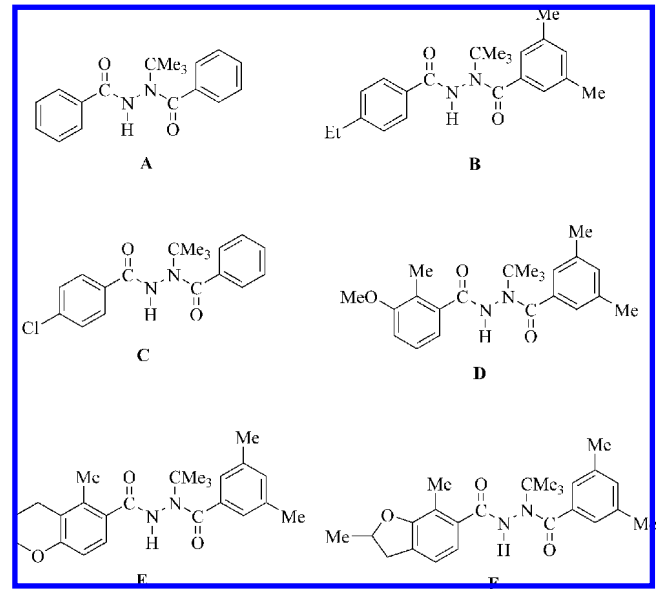
A series of novel *N*-substituted phenoxysulfenyl-*N′*-*tert*-butyl-*N,N′*-diacylhydrazines were designed and synthesized as insect growth regulators via the key intermediates *N*-chlorosulfenyl-*N′*-*tert*-butyl-*N,N′*-diacylhydrazines. Compared to the parent compounds, these *N*-substituted phenoxysulfenyl derivatives displayed better solubility and improved hydrophobicities. The insecticidal activities of the new compounds were evaluated. The results of bioassays showed that the title compounds possessed a combination of strong stomach as well as contact poison property higher than the corresponding parent compounds. In particular, *N*-(4-chlorophenoxy)sulfenyl-*N′*-*tert*-butyl-*N*-4-ethylbenzoyl-*N′*−3,5-dimethylbenzoylhydrazide (**IIIi**) as a field testing candidate has higher stomach toxicities against oriental armyworm and tobacco cutworm than the corresponding parent compound **RH-5992**. Furthermore, the compound **IIIi** exhibits higher contact activities against Asian corn borer, tobacco cutworm, and cotton bollworm than **RH-5992**.

KEYWORDS: *N*-Sulfenate derivative; substituted phenoxysulfenyl; diacylhydrazine; RH-5992; stomach toxicity; contact toxicity; insecticidal activity; insect growth regulator

INTRODUCTION

N-tert-Butyl-*N,N′*-diacylhydrazines, discovered by Rohm and Haas Company, are a class of chemically and mechanistically novel insect growth regulator which have been found to work as nonsteroidal ecdysone agonists inducing, especially in Lepidoptera, precocious molting, leading to death (*1–5*). Because of the unique action mechanism, simple structure, low toxicity to vertebrates, and high insecticidal selectivity, diacylhydrazines have attracted considerable attention for decades (*6–10*). Among these active compounds, *N-tert*-butyl-*N,N′*-dibenzoylhydrazine (**RH-5849**, **A**) was the first to be thoroughly investigated with regard to the insecticidal effects and the functional modes. *N-tert*-Butyl-*N′*-4-ethylbenzoyl-*N*-3,5-dimethylbenzoyl hydrazide (tebufenozide; **RH-5992**, **B**) was the first to be commercialized as a leptidopteran-specific insecticide under the trade names Mimic, Confirm, and Romdan in several countries (*11, 12*). *N-tert*-Butyl-*N′*-4-chlorobenzoyl-*N*-benzoyl hydrazide (halofenozide, **RH-0345, C**), developed by Rohm and Haas Company and American Cyanamid Company, was found to bear



high activity against Coleopteran larvae and ova, though the activity against Lepidoptera was lower than that of tebufenozide (*13*). *N-tert*-Butyl-*N′*-3-methoxy-2-methylbenzoyl-*N*-3,5-dimethylbenzoyl hydrazide (methoxyfenozide, **RH-2485, D**), developed by Rohm and Haas Company, exhibited higher

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

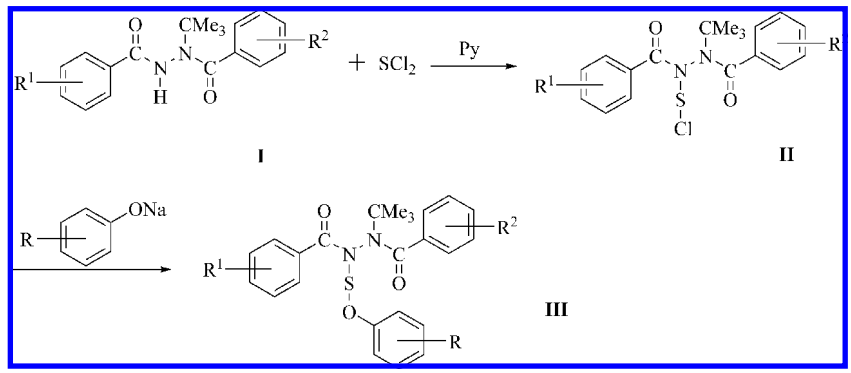


Table 1. Physical Properties and Elemental Analyses of the Compounds **IIIa**−**y**

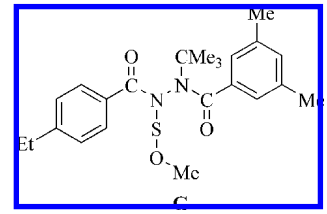
						elemental analysis (%, calcd)		
compd	R	R^1	R^2	mp (°C)	yield (%)	C	H	N
IIIa	H	H	H	85−86	14.9	68.66 (68.55)	5.84 (5.75)	6.91 (6.66)
IIIb	4-Cl	H	H	121−123	42.9	63.49 (63.36)	5.20 (5.10)	6.42 (6.16)
IIIc	4-Me	H	H	145−146	33.3	68.96 (69.10)	5.93 (6.03)	6.49 (6.45)
IIId	H	3,5-Me_2	4-Et	75−77	83.9	70.77 (70.56)	6.51 (6.77)	5.74 (5.88)
IIIe	2-Br	3,5-Me_2	4-Et	122−124	62.6	60.42 (60.54)	5.49 (5.62)	5.09 (5.04)
IIIf	4-Br	3,5-Me_2	4-Et	80−82	82.0	60.62 (60.54)	5.72 (5.62)	5.13 (5.04)
IIIg	2-Cl	3,5-Me_2	4-Et	114−116	64.2	65.71 (65.80)	6.31 (6.11)	5.65 (5.48)
IIIh	3-Cl	3,5-Me_2	4-Et	74−76	46.6	65.70 (65.80)	6.12 (6.11)	5.65 (5.48)
IIIi	4-Cl	3,5-Me_2	4-Et	84−86	85.0	65.70 (65.80)	6.17 (6.11)	5.53 (5.48)
IIIj	2,4-Cl_2	3,5-Me_2	4-Et	126−127	62.3	61.44 (61.65)	5.58 (5.54)	5.14 (5.14)
IIIk	2,4,6-Cl_3	3,5-Me_2	4-Et	121−123	16.2	57.84 (57.99)	5.23 (5.04)	5.01 (4.83)
IIIl	2-Me	3,5-Me_2	4-Et	111−113	26.2	70.83 (70.99)	7.07 (6.98)	5.91 (5.71)
IIIm	3-Me	3,5-Me_2	4-Et	65−67	40	70.86 (70.99)	7.03 (6.98)	5.89 (5.71)
IIIn	4-Me	3,5-Me_2	4-Et	87−89	72.4	70.82 (70.99)	6.79 (6.98)	5.94 (5.71)
IIIo	3,4-Me_2	3,5-Me_2	4-Et	133−135	48.4	71.22 (71.40)	7.20 (7.19)	5.53 (5.55)
IIIp	2-OMe	3,5-Me_2	4-Et	89−92	28.2	68.55 (68.75)	6.69 (6.76)	5.57 (5.53)
IIIq	3-OMe	3,5-Me_2	4-Et	94−96	39.5	68.71 (68.75)	6.71 (6.76)	5.51 (5.53)
IIIr	4-OMe	3,5-Me_2	4-Et	97−99	48.0	68.74 (68.75)	6.54 (6.76)	5.80 (5.53)
IIIs	2-CO_2Me	3,5-Me_2	4-Et	122−124	70.9	67.49 (67.39)	6.28 (6.41)	5.33 (5.24)
IIIt	3-CO_2Me	3,5-Me_2	4-Et	93−95	78.0	67.59 (67.39)	6.25 (6.41)	5.21 (5.24)
IIIu	4-CO_2Me	3,5-Me_2	4-Et	104−106	64.7	67.25 (67.39)	6.60 (6.41)	5.39 (5.24)
IIIv	4-Ph	3,5-Me_2	4-Et	132−134	72.3	73.64 (73.88)	6.69 (6.56)	5.05 (5.07)
IIIw	4-Cl	3,5-Me_2	*a*	72−74	43.1	64.98 (65.14)	5.97 (6.01)	5.21 (5.06)
IIIx	4-Cl	3,5-Me_2	3-OMe, 2-Me	62−64	74.3	64.04 (63.80)	6.07 (5.93)	5.69 (5.31)
IIIy	4-Cl	H	Cl	140−142	62.2	58.86 (58.90)	4.62 (4.53)	5.75 (5.72)

[a] R^1 is identical with the corresponding substituents of the parent compound (**JS-118**).

activity against Lepidoptera and wider insecticidal spectrum than tebufenozide (*14, 15*). Both methoxyfenozide and halofenozide were characterized with significant root systemic activity. It has been reported that *N*′-benzoheterocyclecarbonyl-*N*-*tert*-butyl-3,5-dimethylbenzohydrazide analogues showed high insecticidal activities (*16–18*), of which **ANS-118** and **JS-118** represent successful examples. *N*′-*tert*-Butyl-*N*′-3,5-dimethylbenzoyl-*N*-5-methyl-6-chromane carbohydrazide (Chromafenozide; **ANS-118**, **E**) has been commercialized as insecticide under the trade name Matric (*19, 20*), and *N*′-*tert*-butyl-*N*′-3,5-dimethylbenzoyl-2,7-dimethyl-2,3-dihydrobenzofuran-6-carbohydrazide (**JS-118**, **F**) has been developing by Jiangsu Institute of Agricultural Chemicals, P. R. China (*21, 22*).

However, the preceding diacylhydraines have low solubility in water and limited solubility in common organic solvents. Moreover, they have poor hydrophobicity and cuticular penetration; thus, they have low contact toxicity. These disadvantages impede their field application (*15, 23, 24*).

The activity spectrum of a pesticide is often determined by the physical properties of the compound, and it is possible to develop a new insecticide with improved biological properties 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 (*24–27*). For example, *N*-methoxysulfenyl-*N*′-*tert*-butyl-*N*-4-ethylbenzoyl-*N*′-3,5-dimethylbenzoylhydrazide (**G**), the *N*-methoxy sulfenate derivative of **RH-5992**, showed higher stomach and contact activities than the parent compound **RH-5992** (*28*).



G

It has been reported that phenyl group has better hydrophobicity than short-chain alkyl groups (*29*). Hence, we developed an idea that the introduction of an substituted phenoxysulfenyl substituent into *N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines by substituting the hydrogen on the N′ atom could improve hydrophobicity and biological properties. Herein, we are reporting the synthesis and insecticidal activities of a series of novel N-substituted phenoxysulfenyl-*N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines (**III**) as shown in **Scheme 1**.

Table 2. ^{1}H NMR of Compounds **IIIa**−**y**

compd	δ (ppm)
IIIa	7.44−6.77 (m, 15H, Ph), 1.66 (s, 9H, C(CH_3)$_3$)
IIIb	7.42−6.57 (m, 14H, Ph), 1.67 (s, 9H, C(CH_3)$_3$)
IIIc	7.47−6.60 (m, 14H, Ph), 2.26 (s, 3H, PhCH_3), 1.66 (s, 9H, C(CH_3)$_3$)
IIId	7.12−6.77 (m, 12H, Ph), 2.63 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.21 (s, 6H, Ph(CH_3)$_2$), 1.63 (s, 9H, C(CH_3)$_3$), 1.23 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3),
IIIe	7.50−6.79 (m, 11H, Ph), 2.66 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.24 (s, 6H, Ph(CH_3)$_2$), 1.60 (s, 9H, C(CH_3)$_3$), 1.24 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIf	7.12−6.55 (m, 11H, Ph), 2.64 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.22 (s, 6H, Ph(CH_3)$_2$), 1.66 (s, 9H, C(CH_3)$_3$), 1.22 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIg	7.31−6.77 (m, 11H, Ph), 2.64 (q, $^3J_{HH}$ = 7.8 Hz, 2H, PhCH_2CH$_3$), 2.22 (s, 6H, Ph(CH_3)$_2$), 1.61 (s, 9H, C(CH_3)$_3$), 1.22 (t, $^3J_{HH}$ = 7.8 Hz, 3H, PhCH$_2$CH_3)
IIIh	7.09−6.50 (m, 11H, Ph), 2.64 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.22 (s, 6H, Ph(CH_3)$_2$), 1.66 (s, 9H, C(CH_3)$_3$), 1.22 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIi	7.00−6.60 (m, 11H, ph), 2.64 (q, $^3{}_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.22 (s, 6H, Ph(CH_3)$_2$), 1.66 (s, 9H, C(CH_3)$_3$), 1.23 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3),,
IIIj	7.25−6.54 (m, 10H, Ph), 2.64 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.23 (s, 6H, Ph(CH_3)$_2$), 1.64 (s, 9H, C(CH_3)$_3$), 1.24 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIk	7.04−6.68 (m, 9H, Ph), 2.49 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.25 (s, 6H, Ph(CH_3)$_2$), 1.76 (s, 9H, C(CH_3)$_3$), 1.11 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIl	7.30−6.62 (m, 11H, Ph), 2.67 (q, $^3J_{HH}$ = 7.8 Hz, 2H, PhCH_2CH$_3$), 2.14 (s, 9H, Ph(CH_3)$_2$ and PhCH_3), 1.63 (s, 9H, C(CH_3)$_3$), 1.25 (t, $^3J_{HH}$ =7.8 Hz, 3H, PhCH$_2$CH_3)
IIIm	7.09−6.60 (m, 11H, Ph), 2.63 (q, $^3J_{HH}$ =7.8 Hz, 2H, PhCH_2CH$_3$), 2.20 (s, 9H, Ph(CH_3)$_2$ and PhCH_3), 1.65 (s, 9H, C(CH_3)$_3$), 1.22 (t, $^3J_{HH}$ =7.8 Hz, 3H, PhCH$_2$CH_3)
IIIn	7.00−6.64 (m, 11H, Ph), 2.63 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.26 (s, 3H, PhCH_3), 2.21 (s, 6H, Ph(CH_3)$_2$), 1.64 (s, 9H, C(CH_3)$_3$), 1.23 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3),
IIIo	7.05−6.48 (m, 10H, Ph), 2.63 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.20 (s, 6H, Ph(CH_3)$_2$), 2.16 (s, 3H, PhCH_3), 2.09 (s, 3H, PhCH_3), 1.66 (s, 9H, C(CH_3)$_3$), 1.22 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIp	6.99−6.65 (m, 11H, Ph), 3.71 (s, 3H, OCH$_3$), 2.56 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.25 (s, 6H, Ph(CH_3)$_2$), 1.65 (s, 9H, C(CH_3)$_3$), 1.18 (t, $^3J_{HH}$ =7.5 Hz, 3H, PhCH$_2$CH_3)
IIIq	7.10−6.29 (m, 11H, Ph), 3.70 (s, 3H, OCH$_3$), 2.63 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.21 (s, 6H, Ph(CH_3)$_2$), 1.65 (s, 9H, C(CH_3)$_3$), 1.22 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIr	7.04−6.70 (m, 7H, Ph), 6.67 (d, $^3J_{HH}$ = 9.0 Hz, 2H, Ph), 6.59 (d, $^3J_{HH}$ = 9.0 Hz, 2H, Ph), 3.74 (s, 3H, OCH$_3$), 2.62 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.22 (s, 6H, Ph(CH_3)$_2$), 1.65 (s, 9H, C(CH_3)$_3$), 1.22 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIs	7.76−6.76 (m, 11H, Ph), 3.86 (s, 3H, OCH$_3$), 2.62 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.21 (s, 6H, Ph(CH_3)$_2$), 1.62 (s, 9H, C(CH_3)$_3$), 1.22 (tt, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIt	7.76−6.56 (m, 11H, Ph), 3.91 (s, 3H, OCH$_3$), 2.59 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.21 (s, 6H, Ph(CH_3)$_2$), 1.67 (s, 9H, C(CH_3)$_3$), 1.20 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIu	7.88−6.62 (m, 11H, Ph), 3.90 (s, 3H, OCH$_3$), 2.64 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.22 (s, 6H, Ph(CH_3)$_2$), 1.65 (s, 9H, C(CH_3)$_3$), 1.24 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIv	7.54−7.27 (m, 7H, Ph), 7.07−6.70 (m, 9H, Ph), 2.61 (q, $^3J_{HH}$ = 7.5 Hz, 2H, PhCH_2CH$_3$), 2.22 (s, 6H, Ph(CH_3)$_2$), 1.68 (s, 9H, C(CH_3)$_3$), 1.19 (t, $^3J_{HH}$ = 7.5 Hz, 3H, PhCH$_2$CH_3)
IIIw	7.08−6.50 (m, 9H, Ph), 4.97−4.79 (m, 1H, PhOCH(CH$_3$)CH$_2$), 3.31−3.19 (m, 1H, PhOCH(CH$_3$)CH_2), 2.83−2.68 (m, 1H, PhOCH(CH$_3$)CH_2), 2.27 (s, 6H, Ph(CH_3)$_2$), 1.69 (s, 9H, C(CH_3)$_3$), 1.59−1.41 (m, 6H, PhOCH(CH_3)CH$_2$ and PhCH_3)
IIIx	7.08−6.42 (m, 10H, Ph), 3.78 (s, 3H, OCH$_3$), 2.28 (s, 6H, Ph(CH_3)$_2$), 1.70 (s, 9H, C(CH_3)$_3$), 1.51 (s, 3H, PhCH_3)
IIIy	7.45−7.27 (m, 5H, Ph), 7.16−7.00 (m, 4H, Ph), 6.72−6.49 (m, 3H, Ph), 1.66 (s, 9H, C(CH_3)$_3$)

MATERIALS AND METHODS

Instruments. The title compounds were synthesized under a nitrogen atmosphere. ^{1}H NMR spectra were obtained at 300 MHz using a Bruker AV300 spectrometer or at 400 MHz using a Varian Mercury Plus400 spectrometer in $CDCl_3$ solution with tetramethylsilane as the internal standard. Chemical shift values (δ) are given in ppm. Elemental composition was determined on a Yanaca CHN Corder MT-3 elemental analyzer. The melting points were determined on an X-4 binocular microscope melting point apparatus (Beijing Tech Instruments Co., Beijing, China) and were uncorrected. Yields were not optimized.

General Synthesis. All anhydrous solvents were dried and purified by standard techniques just before use. *N′-tert*-Butyl-*N*,*N′*-diacylhy-

Table 3. Stomach Toxicities against Oriental Armyworm of Compounds **IIIa**−**y** and Parent Compounds

	larvicidal activity (%) at a concentration of				
compd	50 mg kg^{-1}	25 mg kg^{-1}	10 mg kg^{-1}	5 mg kg^{-1}	2.5 mg kg^{-1}
IIIa	100	100	0		
IIIb	100	100	0		
IIIc	100	80	10		
IIId	100	100	100	90	70
IIIe				100	30
IIIf				100	50
IIIg				95	80
IIIh				90	80
IIIi				100	90
IIIj				90	40
IIIk				90	50
IIIl				100	60
IIIm				95	70
IIIn				100	30
IIIo				70	10
IIIp				90	80
IIIq				100	50
IIIr				100	80
IIIs				100	60
IIIt				90	80
IIIu				100	100
IIIv				100	90
IIIw				100	90
IIIx				100	100
IIIy		100	100	30	0
RH-5849	100	70	0	/	/
RH-5992	/	/	100	95	55
JS-118	/	/	/	100	90
RH-2485				100	100
RH-0345	100			70	10

Table 4. Stomach Toxicities against Tobacco Cutworm of Compounds **IIIi** and **RH-5992**

compd	$y = a + bx$	LC_{50} (mg/L)	toxic ratio
IIIi	$y = 1.5640 + 3.6577x$	7.215	1.55
RH-5992	$y = 3.5588 + 1.2691x$	11.178	1

drazines (**I**) were synthesized by the literature method (*3, 23*). Sulfur dichloride was prepared by the reaction of sulfur monochloride with chlorine (*30*). Pyridine was distilled over sodium hydroxide pellets and kept dry by storing over the same reagent.

General Synthetic Procedure for II. To a magnetically stirred and cooled (−20 °C) solution of sulfur dichloride (0.83 g, 8 mmol) in dichloromethane (15 mL) was added dropwise a solution of pyridine (0.63 g, 8 mmol) in dichloromethane (5 mL). After addition was complete, the reaction mixture was stirred below −15 °C for 15 min. Then, a solution of *N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines (**I**) (7 mmol) in dichloromethane (5 mL) was added, and the resulting mixture was stirred at room temperature for 4 h. The solvent was removed in vacuo to afford a viscous residue, and then petroleum ether (60−90 °C) (20 mL) was added. The mixture was stirred at −10 °C for 15 min and then filtered to remove the pyridinium chloride. The filtrate was directly used for the next step without further purification.

General Synthetic Procedure for the Target Compounds IIIa−**y.** To a suspension of sodium hydride (8 mmol) in anhydrous xylene (20 mL) was added substituted phenol (7 mmol) in small portions at room temperature. The reaction mixture was warmed to about 70 °C, and stirring was continued for 2 h and then cooled to −10 °C. The above filtrate of *N*-chlorosulfenyl diacylhydrazine (**II**) was added dropwise, the resulting mixture was stirred at room temperature for 4 h and filtered, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on a silica gel using a mixture of petroleum ether (60−90 °C) and ethyl acetate as the eluent to afford the title compounds **IIIa**−**y**.

Biological Assay. All bioassays were performed on representative test organisms reared in the laboratory. The bioassay was repeated at 25 ± 1 °C according to statistical requirements. Assessments were made on a dead/alive basis, and mortality rates were corrected using Abbott's formula (*31*). Evaluations are based on a percentage scale of 0−100 in which 0 = no activity and 100 = total kill.

Stomach Toxicity against Oriental Armyworm (*Mythimna separata*). The stomach toxicities of the title compounds **IIIa**−**y** and the parent compounds **I** against oriental armyworm were evaluated by foliar application using the reported procedure (*24, 28, 32, 33*). 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 oriental armyworm larvae. Percentage mortalities were evaluated 4 days after treatment. Each treatment was performed three times. For comparative purposes, the parent compounds, **RH-5849**, **RH-5992**, **JS-118**, **RH-2485**, and **RH-0345**, were tested under the same conditions.

Stomach Toxicity against Tobacco Cutworm (*Spodoptera litura*). The stomach toxicities of the title compound **IIIi** and the corresponding parent compound **RH-5992** against tobacco cutworm were tested by leaf-dip method using the reported procedure (*28, 34, 35*). Leaf discs (5 cm × 3 cm) were cut from fresh cabbage leaves and then were dipped into the test solution for 3 s. After air-drying, the treated leaf discs were placed individually into boxes (80 cm^3). Each dried treated leaf disk was infested with five third-instar tobacco cutworm larvae. Percentage mortalities were evaluated 3 days after treatment. Leaves treated with water and acetone were provided as controls. Each treatment was performed three times. For comparative purposes, the parent compound, **RH-5992**, was tested under the same conditions.

Contact Toxicity against Tobacco Cutworm (*Spodoptera litura*), Asian Corn Borer (*Ostrinia furnacalis*), and Cotton Bollworm (*Helicoverpa armigera*). The contact toxicities of the title compound **IIIi** and the corresponding parent compound **RH-5992** against Tobacco cutworm, Asian corn borer, and Cotton bollworm were tested by topical application using the reported procedure (*35–37*). The compounds were dissolved in acetone to prepare five to seven concentrations. For each fourth-instar larva, 1 μL of tested dilution was applied on the thoracic tergite with an automatic microapplicator (Robbins Scientific). Acetone alone served as a control, and **RH-5992** was used as a positive control sample. Usually, 40 insects per dose were tested, and each treatment was replicated four times. After treatment, the insects were returned to their standard rearing conditions. Mortalities were calculated 48 h after treatment, and LD_{50} values (the median lethal dose) were established.

RESULTS AND DISCUSSION

Synthesis. *N*-Substituted phenoxysulfenyl-*N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines (**IIIa**−**y**) were synthesized as shown in **Scheme 1**. *N*-Chlorosulfenyl-*N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines (**II**) were prepared by the reaction of sulfur dichloride with *N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines (**I**) in the presence of pyridine according to our previous work (*28*).

Table 5. Contact Toxicities against Asian Corn Borer, Tobacco Cutworm, and Cotton Bollworm of Compounds **IIIi** and **RH-5992**

	IIIi		RH-5992		
	$y = a + bx$	LD_{50} (μg/g)	$y = a + bx$	LD_{50} (μg/g)	toxic ratio
Asian corn borer	$y = 2.0735 + 1.9932x$	29.393	$y = 3.1305 + 1.0539x$	59.414	2.0
tobacco cutworm	$y = 2.5178 + 1.7545x$	25.986	$y = 1.5124 + 1.2813x$	527.12	20.3
cotton bollworm	$y = 2.1725 + 1.5087x$	74.835	$y = 0.2223 + 1.5321x$	1311.9	17.5

The key intermediates **II** without further purification were reacted with sodium substituted phenoxy to give the title compounds **IIIa**−**y**. We found that the title compounds **III** have better solubility than the parent compound **I** in organic solvents such as methylene dichloride, chloroform, toluene, xylene, petroleum ether, etc., which should make them easier to apply in the field. Moreover, compared to the parent compounds **I**, the hydrophobicities of the title compounds **III** were obviously improved. The physical properties and elemental analyses of the title compounds **IIIa**−**y** are listed in **Table 1**, and their ^{1}H NMR data are listed in **Table 2**.

Bioassay. *Stomach Toxicity against Oriental Armyworm (Mythimna separata).* **Table 3** shows the stomach toxicities of *N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines and their *N*-substituted phenoxysulfeny derivatives **III** against oriental armyworm. The results indicate that the title compounds **III** have excellent stomach toxicities against oriental armyworm, and some of the title compounds **III** exhibit higher larvicidal activities than the corresponding parent compounds. For example, the larvicidal activities of **IIIa** and **IIIb** were 100% at 25 mg kg^{-1}, whereas the corresponding parent compound **RH-5849** caused 70% mortality at this concentration; the larvicidal activities of **IIIg**, **IIIh**, **IIIi**, **IIIp**, **IIIr**, **IIIt**, **IIIu**, and **IIIv** at 2.5 mg kg^{-1} were 80%, 80%, 90%, 80%, 80%, 80%, 100%, and 90%, respectively, as compared with 55% mortality of the corresponding parent compound **RH-5992** at the same concentration. In particular, **IIIi** was sent for advanced testing.

Stomach Toxicity against Tobacco Cutworm (Spodoptera litura). **Table 4** shows the stomach toxicities of the field testing candidate **IIIi** and the corresponding parent compound **RH-5992** against tobacco cutworm. The results indicated that the stomach toxicity of **IIIi** against tobacco cutworm was 1.55-fold as high as that of **RH-5992** from the value of LC_{50}.

The results of the stomach toxicities of the title compounds **III** against oriental armyworm and tobacco cutworm implied that the introduction of the *N*-substituted phenoxysulfenate was essential for the larvacidal activity, and the changes in physical properties might account for the improvement of larvicidal activities.

Contact Toxicity against Tobacco Cutworm (Spodoptera litura), Asian Corn Borer (Ostrinia furnacalis), and Cotton Bollworm (Helicoverpa armigera). **Table 5** shows the contact toxicities of the field testing candidate **IIIi** and the corresponding parent compound **RH-5992** against Asian corn borer, tobacco cutworm, and cotton bollworm. The results indicated that **IIIi** has higher contact activities than **RH-5992**, especially toward tobacco cutworm and cotton bollworm, 20.3 times and 17.5 times, respectively. This could be explained by the marked changes of the physical properties, particularly the decrease of the polarity and the increase of the lipophilicity, both of which lead to the enhancement of cuticular penetration and body assimilation.

In summary, a series of novel *N*-substituted phenoxysulfenyl-*N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines were designed and synthesized as insect growth regulators from the key intermediate *N*-chlorosulfenyl-*N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines. Compared to *N*′-*tert*-butyl-*N*,*N*′-diacylhydrazines, these *N*-substituted phenoxysulfenyl derivatives displayed better solubility and improved hydrophobicities. The results of bioassays showed that the title compounds possessed a combination of strong stomach as well as contact poison properties higher than the corresponding parent compounds. In particular, *N*-(4-chlorophenoxysulfenyl)-*N*′-*tert*-butyl-*N*-4-ethylbenzoyl-*N*′-3,5-dimethylbenzoylhydrazide (**IIIi**), as a field testing candidate, has higher stomach toxicities against oriental armyworm and tobacco cutworm than the corresponding parent compound **RH-5992**. Furthermore, compound **IIIi** exhibits higher contact activities against Asian corn borer, tobacco cutworm, and cotton bollworm than that of **RH-5992**.

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