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Synthesis and Insecticidal Evaluation of *N*-Substituted 2-Nitroiminoimidazolidines

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Abstract: *N*-substituted and *N*,*N*′-disubstituted 2-nitroiminoimidazolidines were prepared from 2-nitroiminoimidazoline. The feeding-contact and systemic activities as insecticides of some of these new compounds have been evaluated. © 1998 Society of Chemical Industry

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Key words: imidacloprid; insecticide; *N*-substituted 2-nitroiminoimidazolidines

1 Introduction

Imidacloprid (Fig. 1: IMI, **1**), which acts on diverse acetylcholine receptors (nAChR) of insect origin, is a relatively new, selective, long-acting neonicotinoid insecticide which can be used with reasonable environmental safety.[1,2] It shows excellent field efficacy even towards insects resistant to the conventional insecticides and is widely used for controlling pests on rice, vegetables and fruit trees.[3]

In this paper, structural modification on the 2-nitroiminoimidazolidine ring are reported and insecticidal properties of some of the new compounds (Fig. 1; **2**, **3**) evaluated.

2 Materials and Methods

2.1 Synthesis of compounds. The synthesis of *N*-substituted and symmetrically *N*,*N*′-disubstituted compounds with structures **2** and **3** was achieved as shown in Fig. 2. Compound **4**, prepared in 58% yield from nitroguanidine and ethylene diamine,[4] could be mono- or dialkylated with halogeno derivatives in acetonitrile under reflux to give **5** and **6**, respectively, in good yields. The attack of two 2-nitroiminoimidazolidine units on the same halogeno derivative could be avoided by using an excess of the latter (2·2 eq. for *N*-monoalkylation, 4·0 eq. for *N*,*N*′-dialkylation). Subsequent treatment of **5** and **6** with silver nitrite in ether containing a few drops of dichloromethane afforded **2** and **3** in good yields.

Unsymmetrical *N*,*N*′-disubstituted compounds **8** and **9** were prepared using a similar methodology (Fig. 3). Each alkylation step was performed with 1·1 eq. of halogeno derivative. Nucleophilic substitution of the

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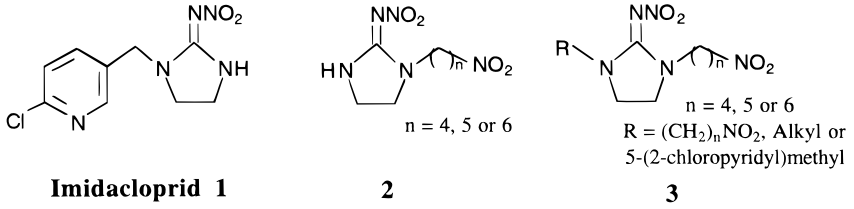

Imidacloprid 1 **2** **3**

Fig. 1. Structures of compounds discussed in text.

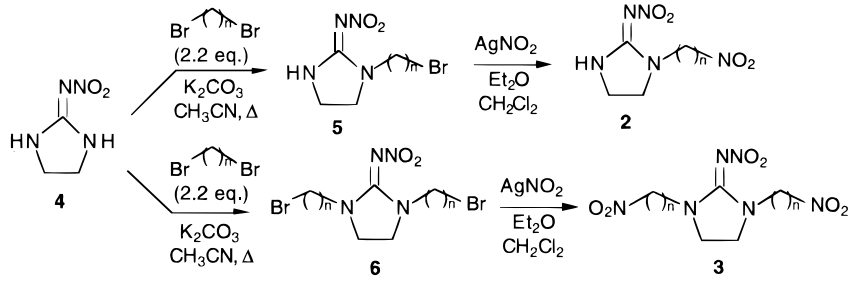

Fig. 2. Synthesis of *N*-substituted and symmetrical *N*,*N*′-disubstituted 2-nitroiminoimidazolidines.

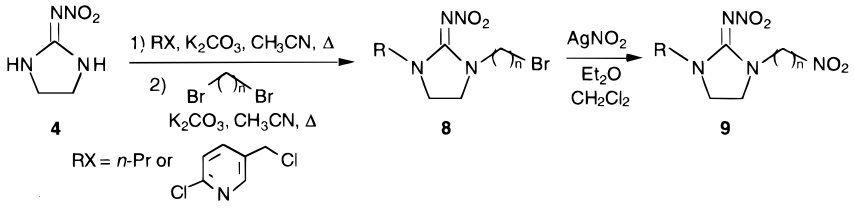

Fig. 3. Synthesis of unsymmetrical *N*,*N*′-disubstituted 2-nitroiminoimidazolidines.

bromine atom with silver nitrite[5] was only possible when R = *n*-Pr.

2.1.1 Preparation of 2-nitroiminoimidazolidine (**4**). 2-Nitroiminoimidazolidine was prepared using nitroguanidine and ethylene diamine according to the method described by McKay and Wright.[4]

2.1.2 General procedure for the alkylation of 2-nitroiminoimidazolidine. The halogeno derivative in acetonitrile (10 ml) was added dropwise to a suspension of 2-nitroiminoimidazolidine (**4**; 1·0 g, 7·69 mmol) and potassium carbonate (1·17 g, 8·46 mmol) in acetonitrile (30 ml). The reaction mixture was refluxed until the starting materials had disappeared (as monitored by TLC), and potassium bromide then filtered off. Evaporation of the solvent afforded a crude product which was purified by column chromatography on silica gel using ethanol + dichloromethane (1 + 99 by volume) as eluent.

2.1.3 General procedure for the nucleophilic substitution of the bromine atom. Silver nitrite (3·27 mmol, 3·2 eq.) was added to the bromo derivative **5**, **6** or **8** (1·02 mmol, 1 eq.) in dry ether containing a few drops of dichloromethane. The mixture was stirred for two days at room temperature in darkness. Silver salts were then filtered off and washed with ether and dichloromethane. Product **2**, **3** or **9** was obtained after evaporation of the solvent mixture under reduced pressure.

2.2 Insecticidal tests. The compounds were tested against the following pests: *Spodoptera littoralis* Boisd. (Egyptian cotton leafworm); *Diabrotica balteata* Le Conte (banded cucumber beetle); *Heliothis viriscens* F. (tobacco budworm); *Aphis. craccivora* Koch (groundnut aphid); *Myzus persicae* Sulz (green peach aphid); *Nilaparvata lugens* Stäol (brown plant hopper) and *Tetranychus urticae* Koch (red spider mite). All compounds were tested initially at 100 and 12·5 mg AI litre^{-1} for feeding-contact and systemic activity, respectively.

S. littoralis: Cotton leaf discs on agar in Petri dishes were sprayed with test solution, allowed to dry and infested with first-instar larvae. The samples were checked one to four days after treatment for mortality, repellent effect, feeding behaviour and growth regulation.

TABLE 1
Synthesis of *N*-substituted 2-Nitroiminoimidazolidines

Compound	*X*	*n*	*Yield* (%)	*m.p.* (°C)	*Purification*
5a	Br	4	42	83	Chromatography
5b	Br	5	72	64	Chromatography
5c	Br	6	62	57	Chromatography
2a	NO_2	4	90	—	Filtration
2b	NO_2	5	68	—	Filtration
2c	NO_2	6	80	—	Filtration
6a	Br	5	47	—	Chromatography
6b	Br	6	51	—	Chromatography
3a	NO_2	5	89	—	Filtration
3b	NO_2	6	94	—	Filtration
Compound	*R*	*R*′	*Yield* (%)	*m.p.* (°C)	*Purification*
7a	2-Chloropyridyl-5-methyl	H	86	127	Chromatography
7b	*n*-Pr	H	85	102	Chromatography
8a	2-Chloropyridyl-5-methyl	$(CH_2)_5Br$	84	—	Chromatography
8b	2-Chloropyridyl-5-methyl	$(CH_2)_6Br$	83	67	Chromatography
8c	*n*-Pr	$(CH_2)_5Br$	80	—	Chromatography
9a	2-Chloropyridyl-5-methyl	$(CH_2)_5NO_2$	0	—	—
9b	2-Chloropyridyl-5-methyl	$(CH_2)_6NO_2$	0	—	—
9c	*n*-Pr	$(CH_2)_5NO_2$	72	—	Filtration

TABLE 2
Insecticidal Activity of Substituted 2-Nitroiminoimidazolidines and Reference Compounds

Pest	*Stage*[b]	*Concentration (mg AI litre*$^{-1}$*)*	*Insecticidal activity*[a]								
			1	***2a***	***2b***	***2c***	***5a***	***5b***	***5c***	***8a***	***8b***
Spodoptera littoralis	L1	100	++	−	−	−	−	−		++	++
Diabrotica balteata	L3	100	++	−	−	−	−	−		++	++
Heliothis virescens	L1	100	++	−	−	−	−	−	−	−	−
Aphis craccivora	m.p.	100	++	−	−	−	−	−	−	−	−
Myzus persicae	m.p.	12·5	++	−	−	−	−	−	−	++	++
Nilaparvata lugens	N3	100	++	−	−	−	−	−	−	++	++
Tetranychus urticae	m.p.	100	−	−	−	−	−	−	−	−	−

[a] ++ >80% mortality; − <30% mortality.
[b] L1: first-instar larvae, L3: third-instar larvae, m.p.: mixed population, N3: third-instar nymph.

D. balteata: Corn seedlings in a Petri dish were treated with test solutions pipetted into the dish and then infested with third-instar larvae. Samples were checked six days after treatment for mortality and growth regulation.

H. virescens: Eggs (0–24 h old) on filter paper were placed in Petri dishes on top of a layer of artificial diet and treated with test solutions introduced by pipette. After six days incubation, samples were checked for egg mortality, larval mortality and growth regulation.

A. craccivora: Pea seedlings, infested with a mixed population were treated with test solutions in a spray chamber. Samples were checked six days after treatment for mortality (contact activity).

M. persicae: Pea seedlings, infested with a mixed population were placed directly in the test solutions. Samples were checked six days after introduction for mortality (systemic activity).

N. lugens: Rice seedlings were treated in a spray chamber with test solution, dried and infested with third-instar nymphs. The samples were checked six to 12 days after the treatment for mortality, growth regulation and effects on F-1 generation.

T. urticae: Bean leaf discs on agar in Petri dishes were infested with a mixed population, and, one day later, were treated with test solution in a spray chamber. Samples were checked for egg mortality, larval mortality, and adult mortality after 10 days incubation.

3 Results and discussion

Table 2 shows the results of insecticidal tests of some new substituted 2-nitroiminoimidazolidines in comparison to imidacloprid (**1**). Compounds **2a**–**c** and **5a**–**c**, were relatively inactive, in contrast to compounds **8a**–**b** which were active at 100 mg AI litre^{-1} (contact) and 12·5 mg AI litre^{-1} (systemic). These results clearly demonstrate that the 5-(2-chloropyridyl)methyl group is necessary for biological activity. The mode of action of **8a**–**b** is probably similar to that of other neonicotinoid insecticides.[6] Further tests were carried out with these compounds, but their activity was clearly poorer than the imidacloprid standard, so the study was discontinued.

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Structure Elucidation of Omphalotin, a Cyclic Dodecapeptide with Potent Nematicidal Activity Isolated from *Omphalotus olearius*

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Abstract: The structure and absolute configuration of omphalotin, a cyclic dodecapeptide isolated from the basidiomycete fungus *Omphalotus olearius* and possessing potent and selective activity against the plant pathogenic nematode *Meloidogyne incognita*, was determined by a combination of