Synthesis and Properties of Thiamethoxam and Related Compounds*

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The neonicotinoids are the most successful chemical class of insecticides reaching sales of more than $1 billion in 2003, mainly due to the excellent market performance of imidacloprid and thiamethoxam. This paper describes the discovery, the synthesis and the insecticidal activity of thiamethoxam and related compounds and reports the hydrolytic stability and the degradation pathways of thiamethoxam together with the synthesis of the degradation products.

Key words: Neonicotinoids, Thiamethoxam, Clothianidin, 4-Nitroimino-1,3,5-oxadiazinanes, Insecticidal Activity

Introduction

An important milestone in the history of modern insect control is marked by the discovery of the neonicotinoid insecticides [1]. As the first representative of this chemical class, imidacloprid **1** was introduced to the market in 1991, and since then, a series of analogues (compounds **2 – 7**) have been launched (Table 1). The neonicotinoids are the fastest growing chemical class of insecticides, now exceeding 15% of the total insecticide market. This tremendous success is based on their unique chemical and biological properties, such as broad-spectrum insecticidal activity, low application rates, excellent systemic characteristics, favourable safety profile, and a new mode of action.

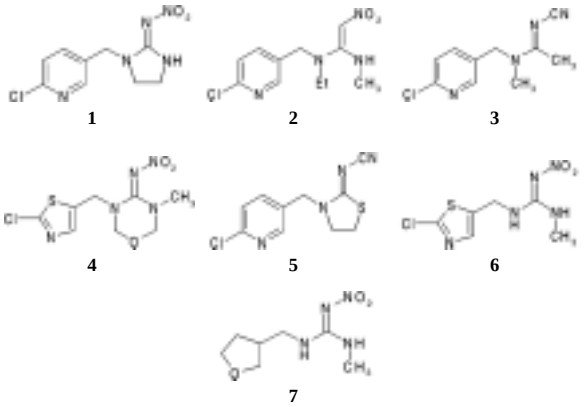
Neonicotinoids bind selectively to insect nicotinic acetylcholine receptors (nAChRs) with nanomolar affinity to act as potent insecticides. However, they do not act as a homogenous class of insecticides. Recent findings suggest that thiamethoxam binds, compared to the other neonicotinoid sales products, in a different way, possibly to a different site of the receptor in aphids [3].

Our own research in this area resulted in the discovery of thiamethoxam (**4**) [4]. This compound is a second-generation neonicotinoid and belongs to the thianicotinyl subclass. It was first synthesized in 1991 and is now developed worldwide for use in more than 100 crops. Thiamethoxam is marketed since 1998 under the trademarks Actara® for foliar and soil treatment and Cruiser® for seed treatment. In all these usages, thiamethoxam provides excellent control of a broad range of commercially important pests, such

Table 1. Neonicotinoid sales products [2].

Common Name	Company	Year of Market Introduction	Sales 2003 Mio $[a]
Imidacloprid (**1**)	Bayer	1991	665
Nitenpyram (**2**)	Takeda	1995	45
Acetamiprid (**3**)	Nippon Soda	1996	60
Thiamethoxam (**4**)	Syngenta	1998	215/298[b]
Thiacloprid (**5**)	Bayer	2000	< 30
Clothianidin (**6**)	Takeda, Bayer	2002	< 30
Dinotefuran (**7**)	Mitsui Chemicals	2002	< 30

[a] Data from Phillips McDougall; [b] sales 2004, data from Syngenta Annual Report 2004.



1 **2** **3**

4 **5** **6**

7

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