Tetrahedron 74 (2018) 336–340

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

A novel and practical method for the synthesis of dinotefuran through Michael addition of nitromethane to diethyl maleate

Haifeng Li, Lailai Wang*

State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000, China

ARTICLE INFO

Article history:
Received 10 October 2017
Received in revised form
24 November 2017
Accepted 1 December 2017
Available online 5 December 2017

Keywords:
Dinotefuran
Synthesis
Mickael addition
Nitromethane
Diethyl maleate

ABSTRACT

A novel and practical synthesis of dinotefuran **1**, featuring a new access to it from known key intermediate (tetrahydrofuran-3-yl)-methanamine **5**, has been achieved through Michael addition reaction of nitromethane to diethyl maleate in 6 steps with 45.5% total yield. This synthesis is scalable and hence has high potential for application to further synthetic elaboration on such new neonicotinoid insecticide dinotefuran **1**.

1. Introduction

Dinotefuran **1**, *N*-methyl-*N*′-nitro-*N*″-(tetrahydro-3-furylmethyl)guanidine, is the most recent synthesized third generation neonicotinoid insecticide.[1–6] It is developed by Mitsui Chemicals (Tokyo, Japan) and first registered in Japan in 2002, and is now increasingly utilized in more than 20 countries.[7–10] The structure of the dinotefuran **1** and its analogs (Fig. 1, **2**–**4**) are very different from the existing nicotine insecticides.[3,8,11] They have a characteristic tetrahydro-3-furylmethyl moiety instead of chloro thiazole (Fig. 1, Second generation neonicotinoids, such as clothianidin **6** and thiamethoxam **7**) and chlorinated pyridine (Fig. 1, First generation neonicotinoids, such as nitenpyram **8**, imidacloprid **9**, acetamiprid **10** and thiacloprid **11**) group of other neonicotinoids, that was previously considered indispensable for insecticidal activity of neonicotinoids.[3,6–9,11–13] At the same time, the properties of dinotefuran are different from nicotine, therefore, it will be known as the "furanicotine".[14]

Dinotefuran is a useful candidate in public health because it shows low mammalian toxicity and broad spectrum quick-kill insecticide which is effective on a wide variety of insect pests such as aphids, shiteflies, leafhoppers, leafminers, sawflies, mole crickets, mealybugs, sawfly larvae and cockroaches.[2–5,10,15,16]

As far as we know, (tetrahydrofuran-3-yl)-methanol and (tetrahydrofuran-3-yl)-methanamine **5** (Fig. 1) are the two important key intermediates in the synthesis of dinotefuran **1**.[9,16] Over the past more than ten years, many studies were performed to synthesize the methanamine **5**. Early synthesis of the methanamine **5** were mainly prepared from mesylated (tetrahydrofuran-3-yl)-methanol.[11,17,18] Among which, the production technique of dinotefuran **1** from (tetrahydrofuran-3-yl)-methanol through alkylation of diethyl malonate and ethyl chloroacetate under alkaline condition has been industrialized, but the route was complicated and hard to operate, the yield was low, and the cost was very high. Liu et al. reported an access to the methanamine **5** in a total yield of 41.1% in 5 steps, with 2, 3-dihydronfuran and trichloroacetyl chloride as starting materials.[19] Chen and Sharpe developed a method to synthesize the methanamine **5**, utilizing Ru/C catalytic hydrogenation, dehydration-cyclization, chlorination, nucleophilic substitution and Raney Ni catalytic hydrogenation from malic acid in an overall yield of 54.7%.[20] Very recently, Zhou et al. described the synthesis of the methanamine **5** through 5 steps starting from 4, 5-dihydrofuran-3-carboxylic acid with 38.0% yield by Pd/C catalytic hydrogenation, chlorination, aminolysis, dehydration and hydrogenation.[21] However, the above methods need long steps, and the application of strongly corrosive, highly toxic and hazardous chemicals would also cause environmental problems. Furthermore, much noble metal catalysts were used and

* Corresponding author.
E-mail address: wll@licp.cas.cn (L. Wang).

https://doi.org/10.1016/j.tet.2017.12.002
0040-4020/

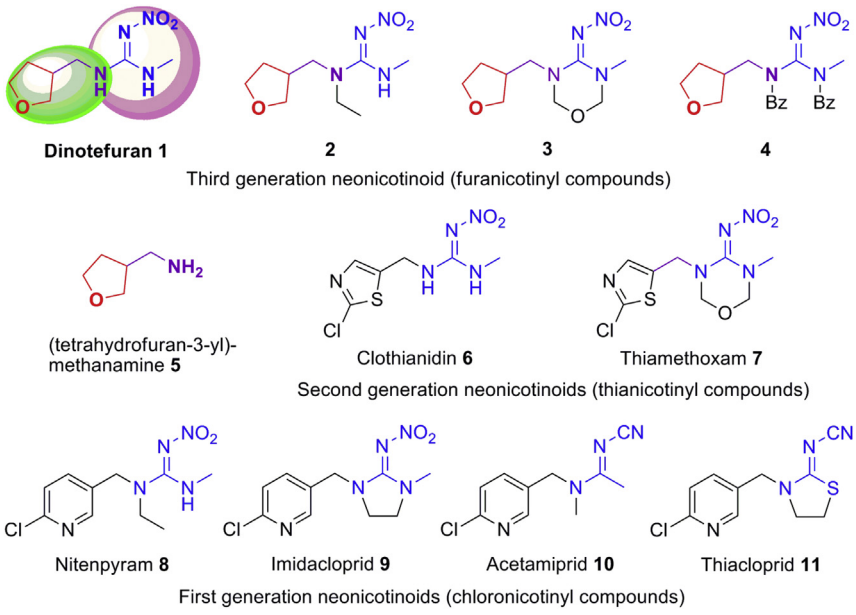
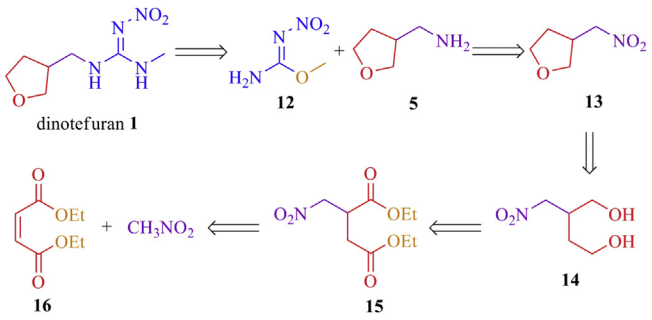


Fig. 1. Structures of dinotefuran **1**, (tetrahydrofuran-3-yl)-methanamine **5**, and other neonicotinoid insecticides **2**–**4** and **6**–**11**.

therefore the cost was high. Thus, it is still imperative to exploit more practical and scalable method to synthesize this methanamine **5**, which has a tetrahydro-3-furylmethyl moiety of dinotefuran **1** and its analogs (Fig. 1, **2**–**4**).

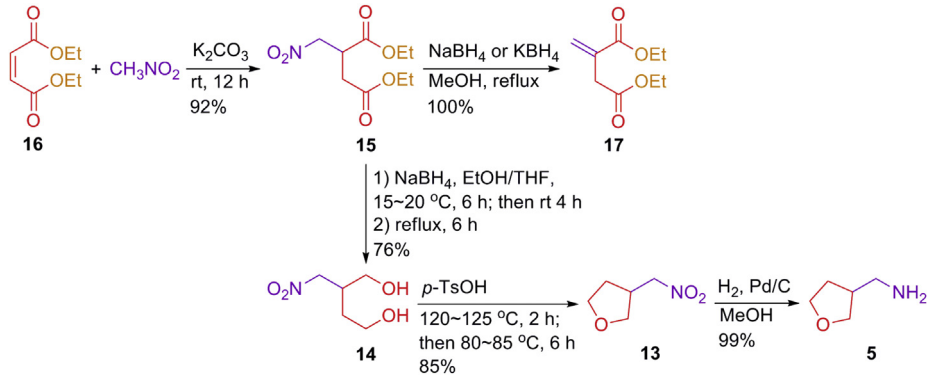
In the present work, our interest has been focused on a novel, practical and scalable method for the synthesis of dinotefuran **1** from (tetrahydrofuran-3-yl)-methanamine **5**, which was synthesized through Michael addition reaction of nitromethane to diethyl maleate.



Scheme 1. Retrosynthetic analysis of dinotefuran **1**.

2. Results and discussion

Our study was mainly focused on the issue of access to the key intermediate (tetrahydrofuran-3-yl)methanamine **5**, which was previously prepared through two steps from another useful intermediate, (tetrahydrofuran-3-yl)methanol, for the synthesis of dinotefuran **1**. In fact, the synthesis of the methanamine **5** not only gave the key intermediate of the third generation neonicotinoid insecticide dinotefuran **1**, but also provided a novel efficient synthesis strategy for the neonicotinoid insecticides which have a characteristic tetrahydro-3-furylmethyl moiety instead of an aromatic heterocyclic ring. As our retrosynthetic analysis outlined in Scheme 1, dinotefuran **1** could be synthesized from *O*-methyl-*N*-nitroisourea **12** and methanamine **5**. The methanamine **5** could be conceived by catalytic hydrogenation of nitrocompound **13**. Next, in a key step, it was thought that nitrocompound **13** could be provided by acid-catalyzed dehydrative cyclization of diol **14**. Diol **14** could be achieved from the nitroester **15** by $NaBH_4$ reduction. We envisioned that nitroester **15** may be obtained from Michael addition reaction of the commercially available nitromethane to diethyl



Scheme 2. Synthesis of the key intermediate (tetrahydrofuran-3-yl)-methanamine **5**.