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Synthesis of N'-Carbamoyl-N-[(6-chloropyridin-3-yl)methyl]ethanimidamide

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ABSTRACT

Acetamiprid is hydrolyzed by using NaOH to get amide derivative of acetamiprid which was further demethylated (Scheme-1). The hydrolysis product of the starting compound has been confirmed on the basis of IR and PMR spectral data.

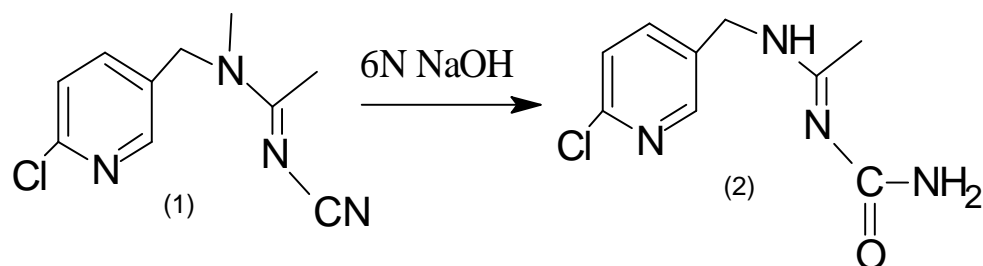
Keywords: Acetamiprid, demethylated acetamiprid, hydrolysis, cynogroup, reported metabolite, corresponding amide.

INTRODUCTION

Acetamiprid, N-[(6-chloro-3-pyridyl)methyl]-N'-cyano-N-methylacetamidine, is a novel insecticide developed by Nippon Soda Co., Ltd to control various noxious insects in agriculture. Mode-of-action studies of acetamiprid suggested that the nicotinic acetylcholine receptor (nAChR) is its primary binding site, as with neonicotinoid insecticides such as imidacloprid. The N-cyanoacetamidine structure of acetamiprid is unique and characteristic since most known neonicotinoids have nitromethylene or nitroimine structures [1]. Acetamiprid has been already well documented. X-ray analysis revealed that the E-geometry along with the imine double bond and syn-relation between the two methyl groups [2].

Acetamiprid, contains cyanoimine functional group, less persistent in acidic medium, while at pH 9.0, first significant changes appeared after the 30 days [3]. Low efficacy of acetamiprid in soil application can be attributed to the fact that acetamiprid could be easily degraded and the partial degraded inter-metabolite demethylated acetamiprid (ACE-dm) remained less bioactive. Therefore, N-demethylation of acetamiprid by some soil bacteria such as *S. maltophilia* might be able to metabolize acetamiprid to ACE-dm. The involvement of P450 in the N-demethylation of some drugs has been reported in human cells [4]. N-demethylation as ACE-dm, the most

prominent metabolite of those analyzed, cyano hydrolysis to ACE-NCONH₂, ACE-dm underwent similar pathways to acetamiprid to yield ACE-dm-NCONH₂ [5]. Metabolic study on mice observed that acetamiprid and ACE-dm in brain, liver, plasma and urine, while ACE-dm-NCONH₂ was observed in urine only [6, 7]. Here, we reported the chemical pathway of hydrolysis of acetamiprid in alkaline condition to get a similar product as reported on natural metabolites of acetamiprid by previous workers.



Scheme-1

EXPERIMENTAL SECTION

N'-Carbamoyl-*N*-[(6-chloropyridin-3-yl)methyl]ethanimidamide (ACE-dmNCONH₂) (2): The solution of acetamiprid (4.44 gm, 0.02 mole) in 30 ml of 6N NaOH and ethanol refluxed for 13 hrs., cooled and neutralized with H₂SO₄, to get a white solid which was filtered and dried. Yield 70%.

IR (KBr) ν 3460, 3423, 3354, 3142, 2871, 2931, 1663, 1567 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 2.88(s, 3H, CH₃), 4.52(s, H, CH₂), 4.56(s, 2H, NH₂), 7.30(d, *J* = 7.5 Hz, 1H, PyH), 7.64(dd, *J* = 8.2 Hz, *J* = 2.5 Hz, 1H, PyH), 8.28(s, 1H, PyH), m/z.

CONCLUSION

The process of alkaline hydrolysis of acetamiprid has been monitored in 6N NaOH. It was observed that N-demethylation occurred followed by the hydrolysis of cyano group to the corresponding amide. This observation is in confirmity with the earlier reported metabolites of hydrolysis of acetamiprid,^{6,7} ACE-dm NCONH₂.

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