

NOTE

Synthesis with Improved Yield and Purity of Amitraz as an Acaricide by New Catalysts

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Amitraz [N-methylbis(2,4-xilyliminomethyl)amine], was synthesized in a one-step manner with improved yield and purity, by new catalysts.

Lead tetraacetate and Silicon tetraacetate were used as single or mixture of them as catalysts. These compounds were added to a mixture of 2,4-dimethylaniline, triethyl orthoformate and N-methyl formamide. After distillation of ethanol and ethylformate timely during the reaction, the temperature was increased and the product was obtained. The results showed that the yield and purity in this method were higher than those in previous methods that had not used catalysts. In addition, the byproducts (ethanol and ethylformate) can be used for other purposes; hence this method is more advantageous and cost-effective.

Key Words: Amitraz, Acaricide, Insecticide, Catalysts, Lead tetraacetate, Silicon tetraacetate.

Amitraz [N-methylbis(2,4-xilyliminomethyl)amine, Fig. 1, I], is a kind of high efficiency and low toxic organic nitrogenous acaricide and insecticide. In 1974, Boots Co. Ltd. in U.K. produced it and its acaricide specific version was reported by Palmer *et al.*¹, for veterinary use and controlling the cattle tick (*Boophilus microplus*) and by Weighton *et al.*² for crop use and spider mite properties.

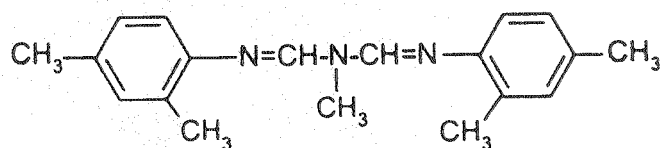


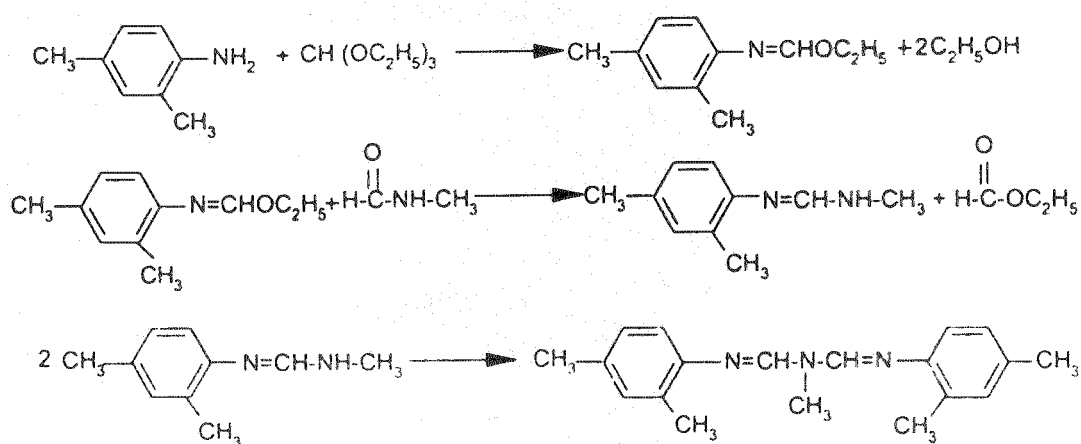
Fig.1. Structure formula of Amitraz

The mode of action probably involves an interaction with octopamine receptors in the tick nervous system, causing an increase in nervous activity and non-systemic, with contact and respiratory action. Expellent action causes ticks to withdraw mouthparts rapidly and fall off the host animal³. This compound controls all the stages of tetranychid and eriophyid mites, pear, suckers, scale

insects, mealybugs, whighefly, aphids and eggs and first instar larvae of lepidoptera on pome fruits citrus fruit, cotton, stone fruit, bush fruit, strawberries, hops, cucurbits, aubergines, capsicums, tomatoes, ornamentals and some other crops⁴⁻⁶.

It is also used as an animal ectoparasiticide to control ticks, mites and lice on cattle, dogs, goats, pigs and sheep⁷ and breaks down rapidly to excretion as a conjugate 4-amino-3-methylbenzoic acid and to a lesser extent to N-(2,4-dimethylphenyl)-N-methylformamidine and 2,4-dimethylformamide⁸⁻¹¹.

This compound has been synthesized by different methods¹²⁻¹⁵, but in our method, a one step reaction (**Scheme-1**) is used for synthesis of Amitraz with



Scheme-1. Schematic reaction for synthesizing Amitraz

better yield and purity compared with the previous methods by new catalysts.

2,4-Dimethyl aniline, triethyl orthoformate, N-methyl formamide, lead tetraacetate, silicon tetraacetate and all other chemical compounds were purchased from Merck Chemical Company (Darmstadt, Germany). Melting point (uncorrected) was determined using a Gallencamp apparatus (CAT. No. 29/MF-370; Watford Herts WD 1852, England) with capillary tube. ¹H NMR spectrum was recorded on a Bruker 80 MHz, Ac-80 spectrometer (Spectrospin, Faellanden, Switzerland) (internal reference TMS). IR spectrum was recorded on a Shimadzu FTIR 4800 spectrophotometer (Kyoto, Japan). Mass spectrum was recorded on a Shimadzu QP-1000 EX spectrometer.

Synthesis of Amitraz

(a) **By use of catalyst lead tetraacetate:** In this reaction, a mixture of 121.18 g (1 mol) 2,4-dimethyl aniline, 163.02 g (1.1 mol) triethyl orthoformate and 35.44 g (0.6 mol) N-methyl formamide and 0.007 mol lead tetraacetate (catalyst A) were reacted in a 500 mL flask and the temperature was increased to distill off ethanol and ethylformate from the reaction vessel. Then the temperature was increased to 180–190°C and the mixture was refluxed for 5 h. The crude was recrystallized in 2-propanol and 23.9 g (75.3%) white yellowish crystals appeared (m.p. 86–88°C) (95.5% purity).

(b) **By use of catalyst silicon tetraacetate:** A mixture of 121.18 g (1 mol) 2,4-dimethyl aniline, 163.02 g (1.1 mol) triethyl orthoformate and 35.44 g (0.6 mol) N-methyl formamide and 0.007 mol silicon tetraacetate (catalyst B) were reacted in a 500 mL flask, and the temperature was increased to distill off ethanol and ethylformate from the reaction vessel. Then the temperature was increased to 180–190°C and the mixture was refluxed for 5 h. The crude was recrystallized in 2-propanol and 23 g (74.2%) white yellowish crystals appeared (m.p. 86–88°C) (96.2% purity).

IR (KBr cm^{-1}): 3435, 2917.9, 2933, 1621.8, 1598.4, 1494.38, 1293.5, 1200.8, 1080.7. $^1\text{H NMR}$ (CDCl_3) (ppm): 2.27 (6H, s, 2CH_3), 2.36 (6H, s, 2CH_3), 3.51 (3H, s, NCH_3), 6.75 (1H, d, $J = 7.0$ Hz, CH), 6.95 (1H, dd, $J = 7.0$ Hz and $J = 1.5$ Hz, CH), 7.05 (1H, d, $J = 1.5$ Hz, CH), 7.95 (2H, s, $2\text{CH} = \text{N}$); Mass spectra MS: m/e (regulatory intensity): 292 (13.1), 162 (100), 147 (8.6), 132 (11.7), 121 (84.9), 106 (30.1), 77 (46.8), 57 (24.4), 42 (2.0).

Amitraz [N-methylbis(2,4-xylyliminomethyl)amine] is one of the high usage acaricides and insecticides that is particularly active against cattle, tick and red spider mite¹⁶. This compound has the general formula:



in which X and Y, which may be identical or different and are 2,3-dimethylphenyl, 2,4-dimethylphenyl, 2,6-dimethylphenyl, 2,4,6-trimethylphenyl, 2,4,5-trimethylphenyl, 2,3,4-trimethylphenyl, 2-methyl-4-halophenyl, 2-ethyl-4-halophenyl, 2-halo-4-methylphenyl, 2-halo-4,6-dimethylphenyl, 2,4-dihalo-6-methylphenyl and 2-methyl-4-methoxyphenyl. These compounds have valuable pesticidal properties. For example, these compounds have acaricidal properties, as shown by their activity against the larvae of cattle ticks, viz., the larvae of *Boophilus microplus*⁷.

The effect of temperature and time of reaction on yield was tested. It was found that when the temperature was lower than 160°C, the reaction rate and the yield of Amitraz were very low. However, when the reaction was a little fast at 170°C and at 180°C, the reaction was almost completed with high yield. When the temperature was more than 200°C, the colour of reaction (Amitraz crude) became dark and no development in production yield; so the best reaction temperature should be 180–190°C.

The different reaction times under other reaction conditions were also tested. It was found that the reaction was not finished within 3 h and the yield of Amitraz in this time was low, but after 5 h there was no difference in yield as time went on.

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