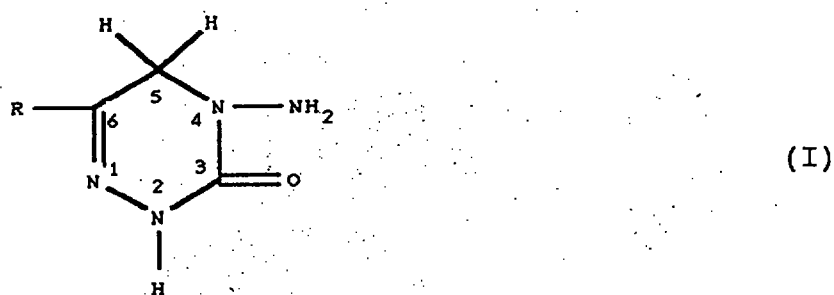


PS/5-17831/=

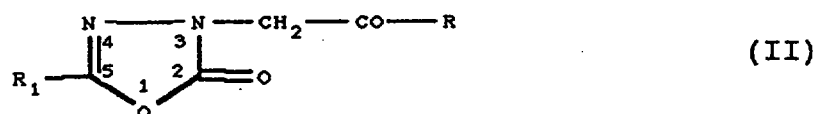
Process for the preparation of aminotriazine derivatives

The present invention relates to a novel process for the preparation of 4-amino-3-oxo-2,3,4,5-tetrahydro-1,2,4-triazines.

The invention relates to a process for the preparation of a compound of formula I



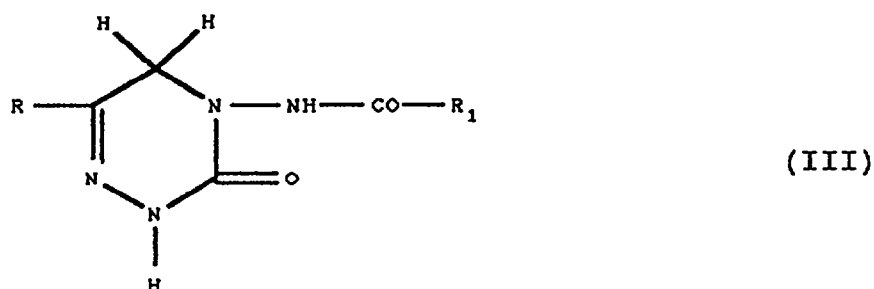
wherein R is hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₁-C₄alkyl substituted by from 1 to 10 halogen atoms or by from 1 to 3 radicals from the group C₁-C₃alkoxy, C₁-C₃alkylthio and phenyl, phenyl or phenyl substituted by from 1 to 3 radicals from the group halogen, methyl, ethyl, methoxy, methylthio and nitro, which process comprises reacting with hydrazine hydrate a compound of formula II



wherein R₁ is hydrogen, C₁-C₄alkyl, C₃-C₆cycloalkyl, C₁-C₄alkyl substituted by from 1 to 9 chlorine atoms, C₁-C₃alkoxy, C₁-C₃alkylthio, C₁-C₃alkylsulfinyl, C₁-C₃alkylsulfonyl,

phenyl, phenyl substituted by from 1 to 3 radicals from the group halogen, methyl, ethyl, methoxy, methylthio and nitro, or pyridyl, and

R is as defined above; and subjecting the resulting compound of formula III



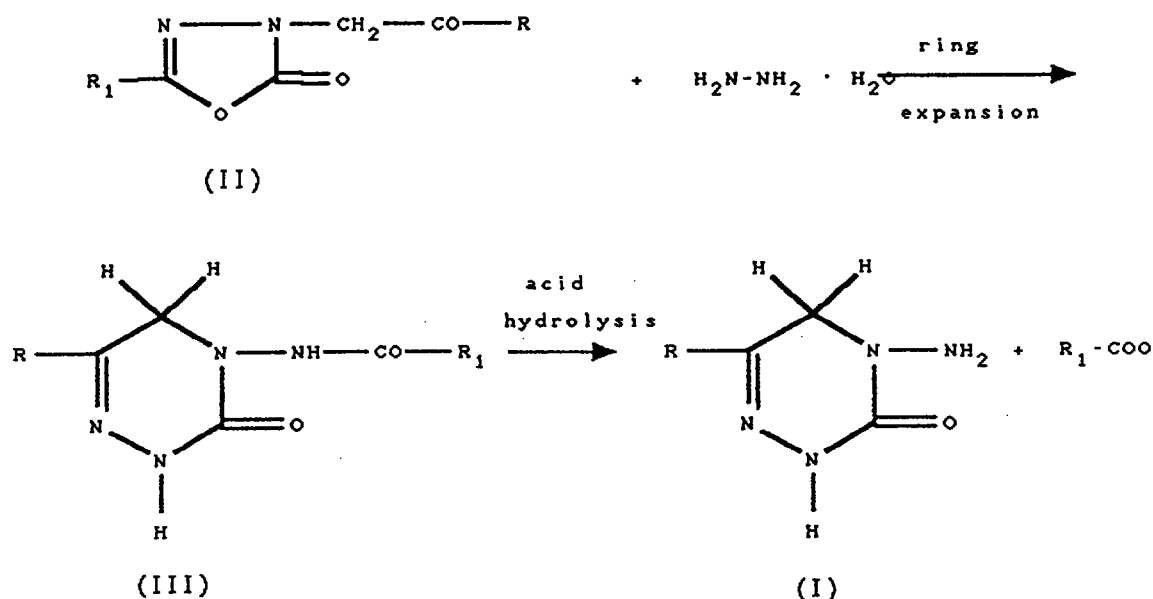
to hydrolysis, preferably acid hydrolysis.

The present process is preferably used for the preparation of compounds of formula I wherein R is methyl, ethyl, isopropyl, tert.-butyl or cyclopropyl. The process is preferably carried out using compounds of formula II wherein R₁ is C₁-C₄alkyl as starting materials.

The aminotriazine derivatives of formula I prepared according to the invention can be used as intermediates for the preparation of 4-[(pyrid-3-yl)-methylenamino]- or 4-[(pyrid-3-yl)-methylamino]-3-oxo-2,3,4,5-tetrahydro-1,2,4-triazines, which are distinguished by pronounced insecticidal and acaricidal activity. Such pesticidal compounds that may be mentioned are, for example, 4-[(pyrid-3-yl)-methylenamino]-3-oxo-6-methyl-2,3,4,5-tetrahydro-1,2,4-triazine, 4-[(pyrid-3-yl)-methylenamino]-3-oxo-6-cyclopropyl-2,3,4,5-tetrahydro-1,2,4-triazine, 4-[(pyrid-3-yl)-methylamino]-3-oxo-6-isopropyl-2,3,4,5-tetrahydro-1,2,4-triazine and 4-[(pyrid-3-yl)-methylamino]-3-oxo-6-tert.-butyl-2,3,4,5-tetrahydro-1,2,4-triazine. Such pesticidal compounds, their preparation and use are described in EP Patent Application

314,615.

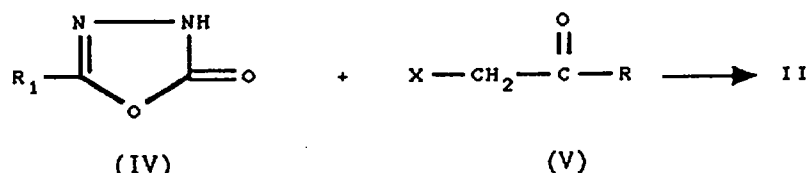
The process according to the invention can be illustrated by the following reaction scheme, the radicals R and R₁ being as defined above:



The first step (ring expansion) of the process according to the invention for the preparation of the compounds of formula I is usually carried out under normal pressure and preferably in a solvent. The temperature is from +15 to 120°C, preferably from +20 to 100°C. Suitable solvents are, for example, water, nitriles, such as acetonitrile, alcohols, dioxane or tetrahydrofuran. The subsequent hydrolysis of the acylamino compounds of formula III to the free amino compounds of formula I is preferably carried out with inorganic acids, such as 1N hydrochloric acid to conc. hydrochloric acid or 1N to 10N sulfuric acid, at temperatures of from 0 to 120°C, especially from +20 to 100°C, in an aqueous medium or in inorganic solvents, such as alcohols, dioxane, tetrahydrofuran, nitriles, etc..

The 1,3,4-oxadiazolon-3-yl-ketones of formula II used as

starting materials according to the invention are novel. They can be prepared analogously to known procedures, for example as follows (see, for example, EP Patent Application No. 314,615):

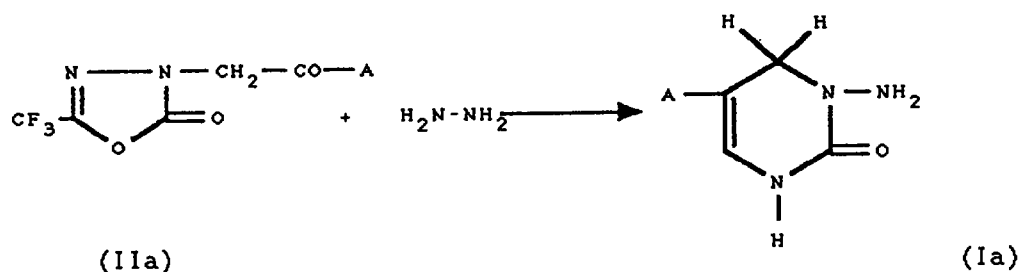


In the above formulae IV and V, R and R₁ are as defined above and X is a halogen atom, preferably chlorine or bromine. The above process for the preparation of the oxadiazolone ketones of formula II is generally carried out under normal pressure in the presence of a base and in a solvent. The temperature is from 0 to +150°C, preferably from +20 to 100°C. Suitable bases are organic and inorganic bases, for example trimethylamine, alcoholates, sodium hydroxide or sodium hydride. Suitable solvents are, *inter alia*, alcohols, halogenated hydrocarbons, for example chloroform, nitriles, for example acetonitrile, tetrahydrofuran, dioxane, dimethyl sulfoxide, dimethylformamide or water.

The oxadiazolones of formula IV [see EP Patent Application No. 321,833; J. Pharm. Soc. Japan 76, 1300-1303 (1956); Vol. 82, 121-123 (1949)] and their preparation, and also the halo-ketones of formula V, are for the most part known.

It is known from Liebigs Ann. Chem. 749, 125 ff. (1971) that 4-amino-6-phenyl-3-oxo-2,3,4,5-tetrahydro-1,2,4-triazines can be obtained starting from 2-amino-5-methyl-3-phenacyl-1,3,4-oxadiazolium bromide by reaction with hydrazine hydrate. The main disadvantage of this process is that it is limited to the preparation of 1,2,4-triazine rings that are phenyl-substituted in the 6-position; in addition, the process comprises several steps and its yield is poor. Furthermore,

it is known from EP Patent Application No. 314,615 to prepare 4-amino-3-oxo-2,3,4,5-tetrahydro-1,2,4-triazines that are substituted in the 6-position, by reacting corresponding 5-trifluoromethyl-1,3,4-oxadiazolon-3-yl-ketones with excess hydrazine in a one-step reaction:



wherein A may be an unsubstituted or substituted alkyl or aryl substituent. The disadvantages of this process are primarily the high cost of the trifluoroacetic acid ethyl ester required for preparing the trifluoroacethydrazide, the instability of that trifluoroacethydrazide at room temperature, and the not very high yield in the reaction of the trifluoroacethydrazide with phosgene in water (see *Helv. Chim. Acta* 1986, 333) to prepare the 5-trifluoromethyl-1,3,4-oxadiazol-2(3H)-one from which the 5-trifluoromethyl-1,3,4-oxadiazolon-3-yl-ketones of formula IIa above (starting compound) are obtained. Moreover, the reaction according to EP Patent Application No. 314,615 inevitably produces toxic trifluoroacetic acid derivatives as a by-product, which present ecological problems and require a considerable outlay for their disposal.

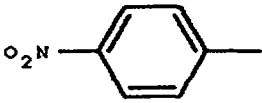
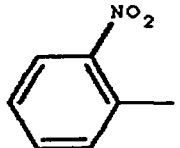
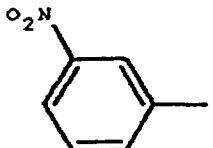
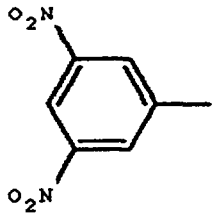
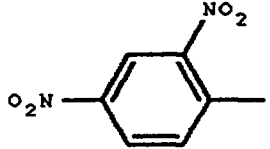
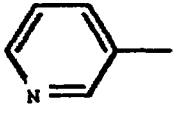
In contrast, within the scope of the present invention it has now surprisingly been found that the presence of a 5-CF₃ group in the starting compounds of formula II is not necessary for the preparation of the 4-amino-3-oxo-2,3,4,5-tetrahydro-1,2,4-triazines of formula I by ring expansion. The present starting compounds of formula II, which contain

one of the mentioned radicals R_1 in the 5-position instead of the mentioned CF_3 group, react readily with hydrazine hydrate to form the acylamino compounds of formula III, from which, however, the radical $-CO-R_1$ must subsequently be removed by acid hydrolysis to obtain the compounds of formula I. With the process according to the invention, the disadvantages of the procedures hitherto available are eliminated since, in the process according to the invention, inexpensive and readily available starting compounds can be used, high yields are obtained and, instead of toxic trifluoroacetic acid derivatives, ecologically harmless carboxylic acid derivatives, for example acetic acid, are formed as a by-product.

Example 1: Preparation of the starting compound
2,3-Dihydro-5-methyl-2-oxo-1,3,4-oxadiazole-3-acetone

10 g of 2,3-dihydro-5-methyl-2-oxo-1,3,4-oxadiazole (prepared in customary manner from acethydrazide and phosgene) are added to a solution of 2.3 g of sodium in 100 ml of methanol, the mixture is stirred for a short time and then the solvent is removed in vacuo at a bath temperature of 60°C. The sodium salt so formed is introduced in portions into a solution of 9.2 g of chloroacetone and 0.2 g of tetrabutylammonium bromide in 50 ml of chloroform, and the reaction mixture is stirred for 4 hours at 65°C. After the salts have been filtered off, the solvent is removed in vacuo at a bath temperature of 50°C. The residue that remains is recrystallised from tert.-butyl methyl ether, yielding the title compound having a melting point of 55-57°C.

The following compounds of formula II are also prepared in a manner corresponding to that described above:

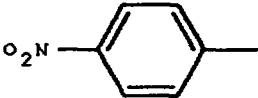
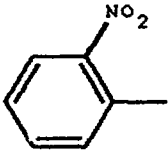
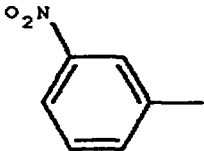
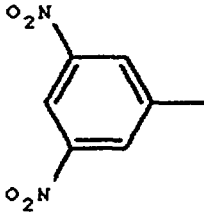
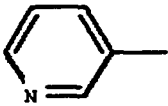
R_1	R	phys. data
H	-CH ₃	b.p. 0.08 torr/80°C
-CH ₃	-CH ₃	m.p. 55-58°C
-C(CH ₃) ₃	-CH ₃	b.p. 0.07 torr/102°C
	-CH ₃	m.p. 179-181°C
	-CH ₃	m.p. 98-102°C
	-CH ₃	m.p. 126-129°C
	-CH ₃	m.p. 116-118°C
	-CH ₃	m.p. 164-168°C
	-CH ₃	m.p. 146-148°C
-CH ₃	-CF ₃	
-CCl ₃	-CH ₃	

Example 2:

a) Preparation of 4-acetylamino-6-methyl-3-oxo-2,3,4,5-tetrahydro-1,2,4-triazine (ring expansion):

3.12 g of the 2,3-dihydro-5-methyl-2-oxo-1,3,4-oxadiazole-3-acetone prepared according to Example 1 are stirred in 40 ml of alcohol together with 2 g of hydrazine hydrate for 16 hours at a bath temperature of 35°C. After the solvent and the excess hydrazine have been evaporated off in vacuo, recrystallisation from isopropanol yields the title compound having a melting point of 197-199°C.

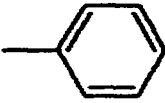
The following compounds of formula III are also prepared in a manner corresponding to that described above:

R_1	R	m.p. [°C]
H	-CH ₃	185-187°
-CH ₃	-CH ₃	197-199°
-C(CH ₃) ₃	-CH ₃	205-207°
	-CH ₃	252-255°
	-CH ₃	255-257°
	-CH ₃	228-231°
	-CH ₃	259-262°
	-CH ₃	259-262°
-CH ₃	H	
-CH ₃	-CF ₃	
H	H	

b) Preparation of 4-amino-6-methyl-3-oxo-2,3,4,5-tetrahydro-1,2,4-triazine (acid hydrolysis):

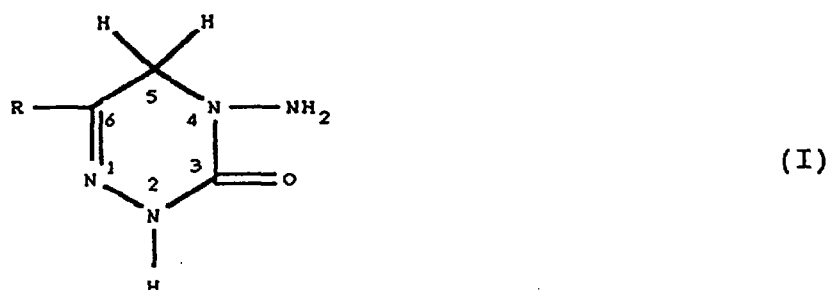
1.7 g of the 4-acetylamino-6-methyl-3-oxo-2,3,4,5-tetrahydro-1,2,4-triazine prepared according to a) above are stirred for 5 hours in 10 ml of 2N hydrochloric acid at 80°C. After cooling of the solution, 1.7 g of sodium acetate are added and the solution is concentrated by evaporation in a rotary evaporator at a bath temperature of 60°C. The residue formed is stirred with ethanol and freed of salt precipitates by filtration. The resulting solution is concentrated to a small volume and caused to crystallise. The title compound is obtained in the form of colourless crystals having a melting point of 116-119°C.

The following compounds of formula I are also prepared in a manner corresponding to that described above:

R	m.p. [°C]
-CH ₃	116-119°
-C ₂ H ₅	143-145°
-C ₃ H ₇ (i)	79- 81°
-C(CH ₃) ₃	148-150°
	94- 95°
	199-202°
	208-210°
H	
-CF ₃	

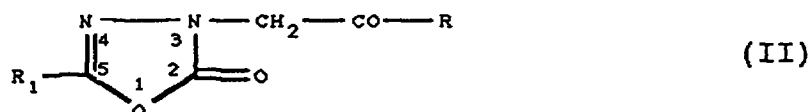
What is claimed is:

1. A process for the preparation of a compound of formula I



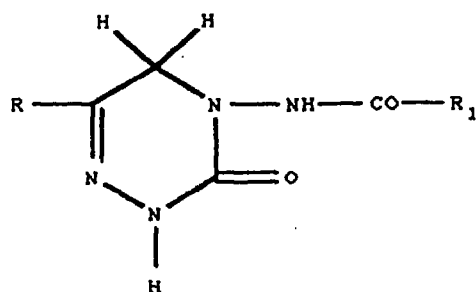
wherein

R is hydrogen, C₁-C₆alkyl, C₃-C₆cycloalkyl, C₁-C₄alkyl substituted by from 1 to 10 halogen atoms or by from 1 to 3 radicals from the group C₁-C₃alkoxy, C₁-C₃alkylthio and phenyl, phenyl or phenyl substituted by from 1 to 3 radicals from the group halogen, methyl, ethyl, methoxy, methylthio and nitro, which process comprises reacting with hydrazine hydrate a compound of formula II



wherein R₁ is hydrogen, C₁-C₄alkyl, C₃-C₆cycloalkyl, C₁-C₄-alkyl substituted by from 1 to 9 chlorine atoms, C₁-C₃alkoxy, C₁-C₃alkylthio, C₁-C₃alkylsulfinyl, C₁-C₃alkylsulfonyl, phenyl, phenyl substituted by from 1 to 3 radicals from the group halogen, methyl, ethyl, methoxy, methylthio and nitro, or pyridyl; and

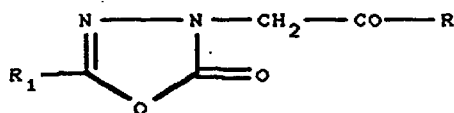
R is as defined above; and subjecting the resulting compound of formula III



(III)

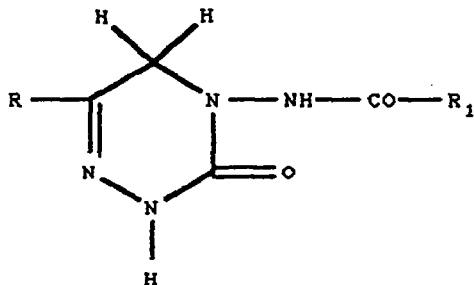
to hydrolysis.

2. A process according to claim 1, wherein the compound of formula III is subjected to acid hydrolysis.
3. A process according to claim 1 or 2, wherein the compound of formula III is subjected to hydrolysis with an inorganic acid.
4. A process according to any one of claims 1 to 3 for the preparation of a compound of formula I wherein R is methyl, ethyl, isopropyl, tert.-butyl or cyclopropyl.
5. A process according to any one of claims 1 to 4, wherein a compound of formula II wherein R₁ is C₁-C₄alkyl is reacted.
6. A compound of formula II according to claim 1



(II).

7. A compound of formula III according to claim 1



(III).