

**Russian Academy of Sciences**

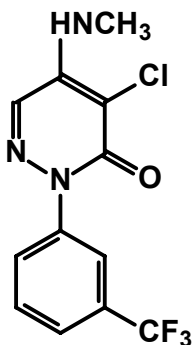
**A. N. Nesmeyanov Institute of Organoelement Compounds of RAS,  
Vavilov St. 28, 119991 Moscow, Russia**

**Novel three-component reaction as a route to the synthesis  
of 4-trifluoromethylpyridazin-3-ones**

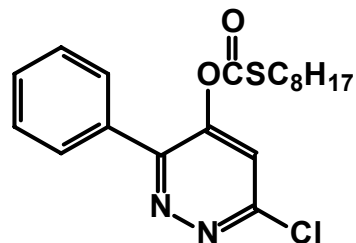
**V.I.Dyachenko\*, A.S.Peregudov, N.D.Chkanikov**

**Moscow - 2006**

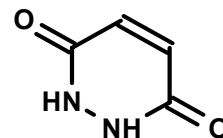
## Herbicides activity of piridazines



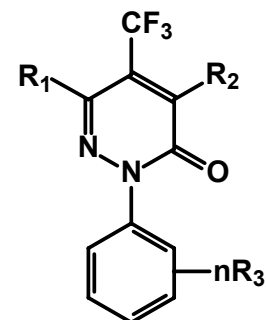
**Norflurazon**



**Piridat**

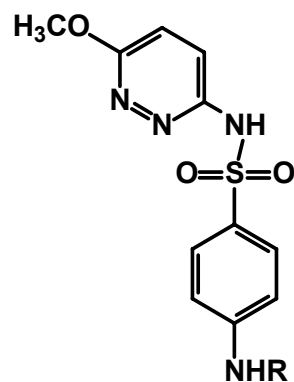


**Maleic hydrazide**

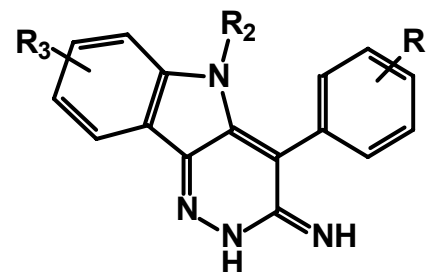
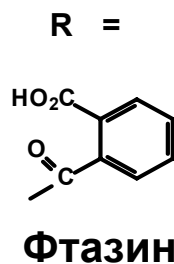


**1**

## Antibacterial activity



**R = H Сульфapiридазин**



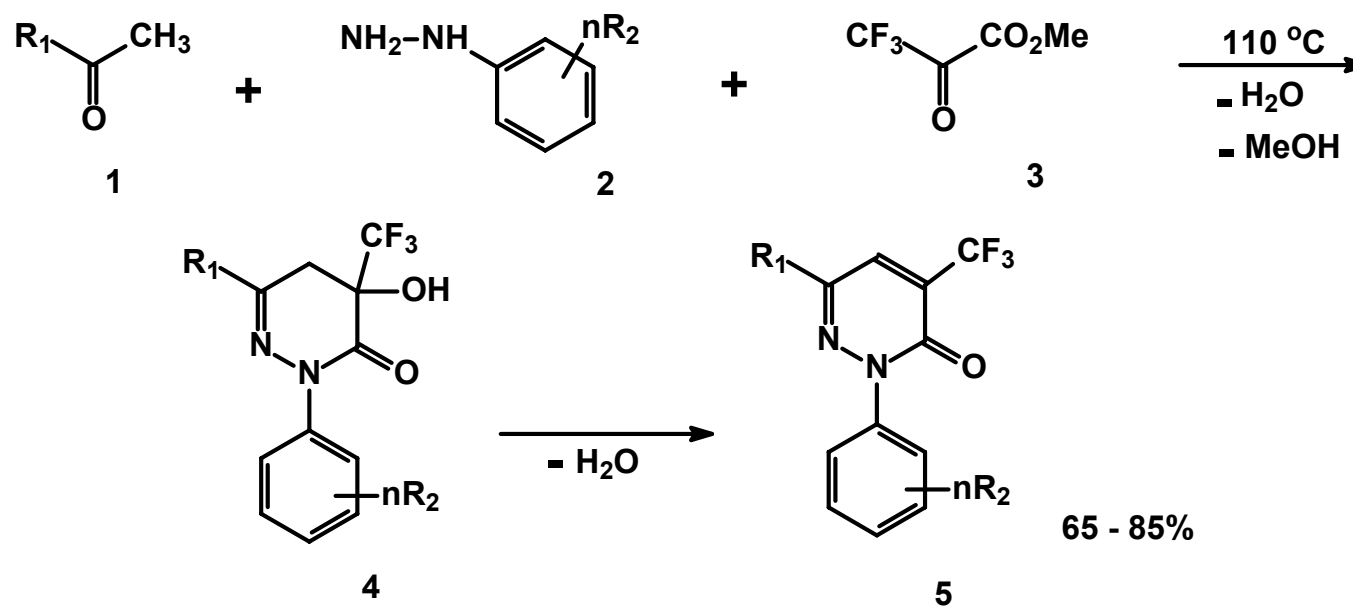
**2**

**antituberculosis activity**

1. Katayama et al./ US. Patent № 6,482,773 B1, 2002

2. Velezheva V.S. et al./J. Med. Chem.,47; 13; 2004; 3455-3461

## Novel Three-component Reaction as a rout synthesis of 4-trifluoromethylpyridazin-3-ones

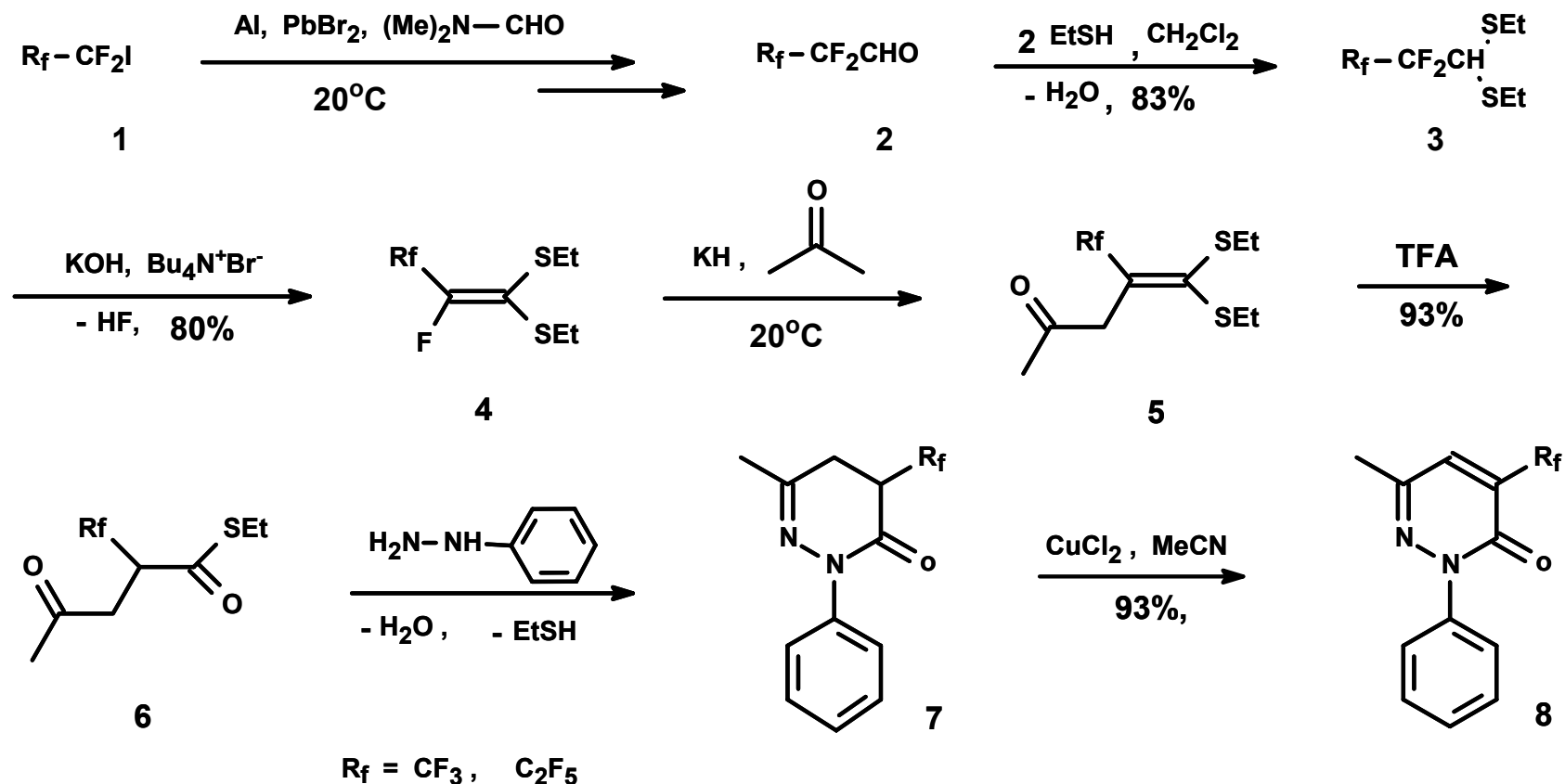


$\text{R}_1 = \text{Alk, Ar, Heter}$

$\text{R}_2 = \text{Me, OMe, Cl, F, Br, NO}_2$

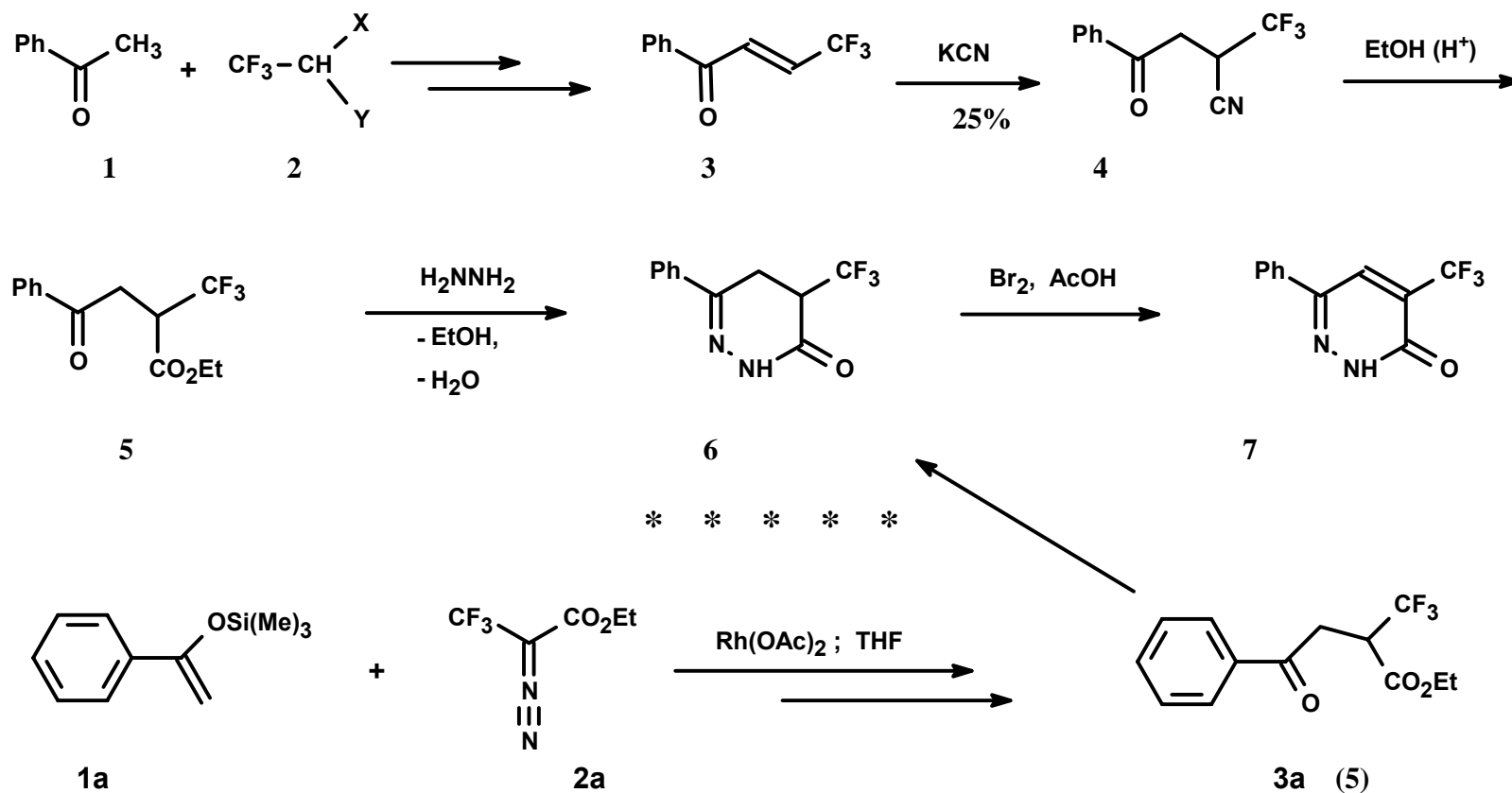
$n = 0 - 3$

# The know rout synthesis of 4-trifluoro-piridazin-3-ones (№1)



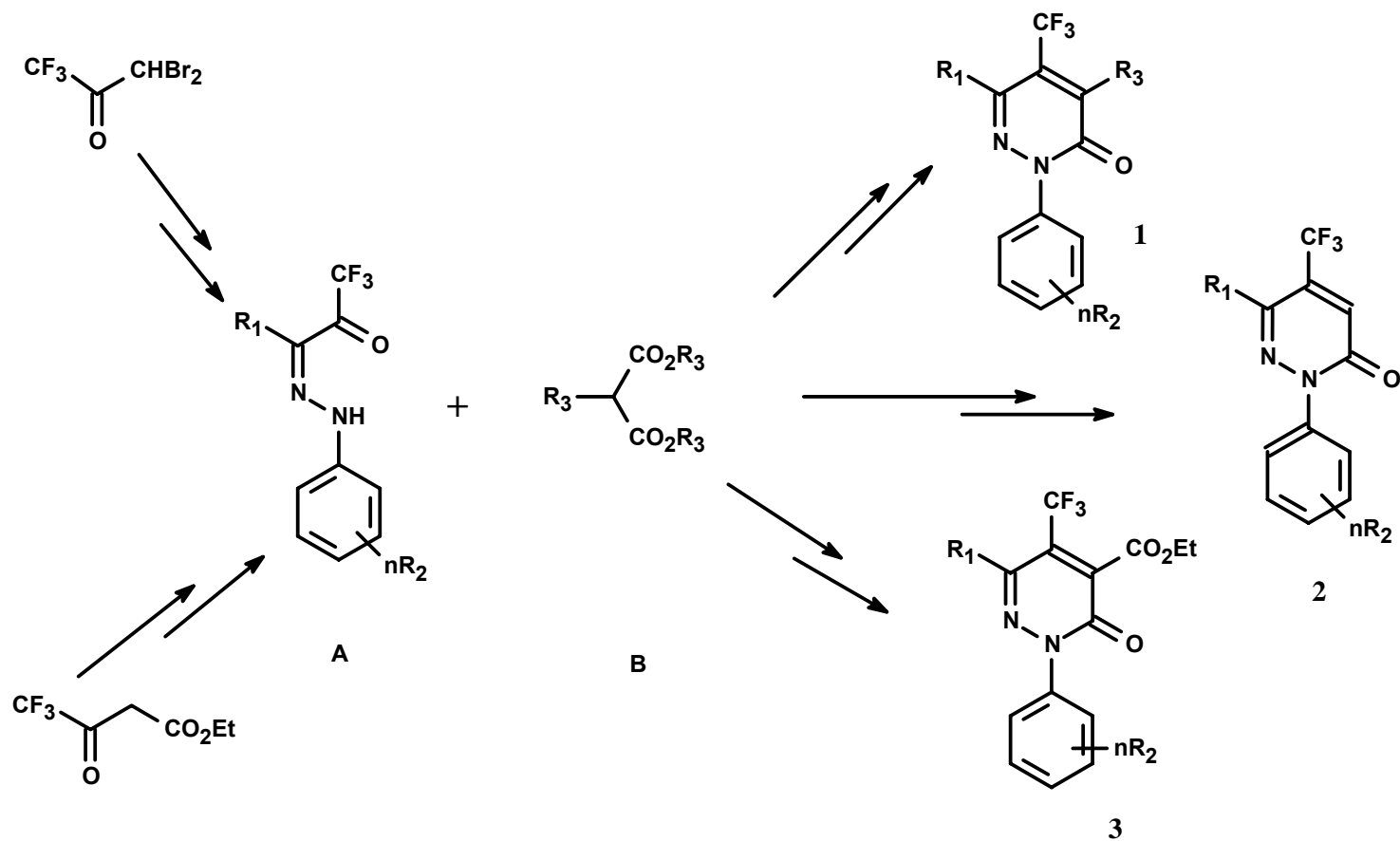
1. Muzard, Murielle; Portella, Charles; J. Org. Chem.; 58; 1; 1993; 29-31.
2. Bouillon, Jean-Philippe; Henin, Beatrice; Huot, Jean-Francois; Portella, Charles; Eur. J. Org. Chem.; 9; 2002; 1556 - 1561.
3. Brule, Cedric; Bouillon, Jean-Philippe; Nicolai, Eric; Portella, Charles; Synthesis; 3; 2003; 436-442.

## Know rout synthesis of 4-trifluoro-piridazin-3-ones №2



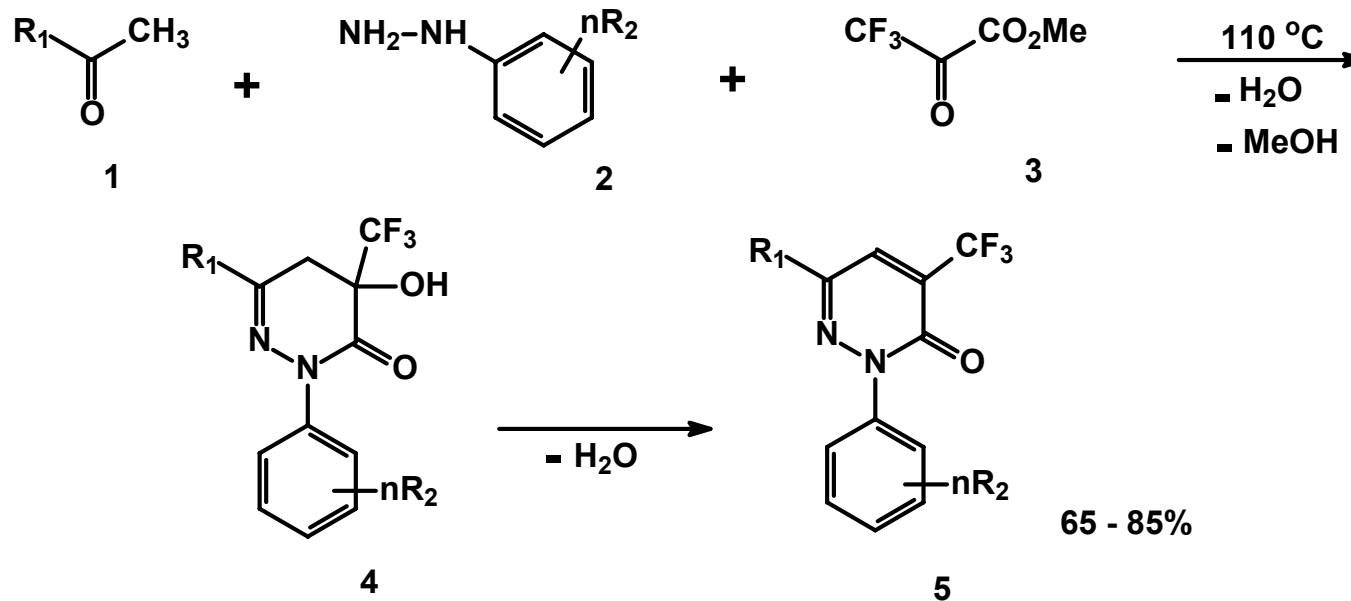
- Contreras, Jean-Marie; Rival, Yveline M.; Chayer, Said; Bourguignon, Jean-Jacques; Wermuth, Camille G.; J. Med. Chem.; EN; 42; 4; 1999; 730 - 741.
- Schi, Guopiang; Xu, Yuanyao; JOCEAH; J. Org. Chem.; EN; 55; 10; 1990; 3383-3386.

## Know a rout synthesis of 5-trifluoro-piridazin-3-ones



1. Katayama et al./ US. Patent № 6,482,773 B1, 2002

## Novel Three-component Reaction as a rout synthesis of 4-trifluoromethylpyridazin-3-ones

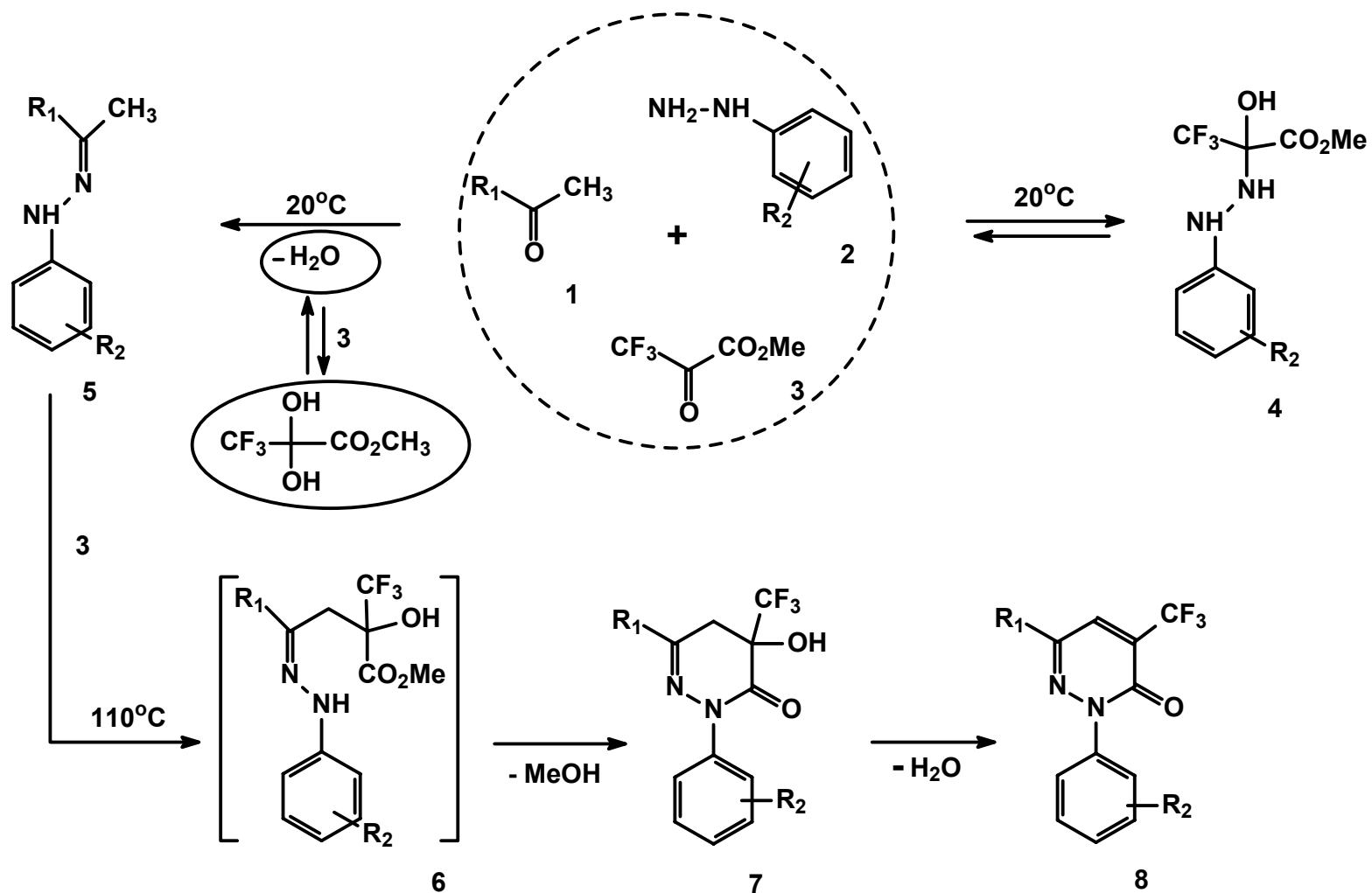


$R_1$  = Alk, Ar, Heter

$R_2$  = Me, OMe, Cl, F, Br,  $NO_2$

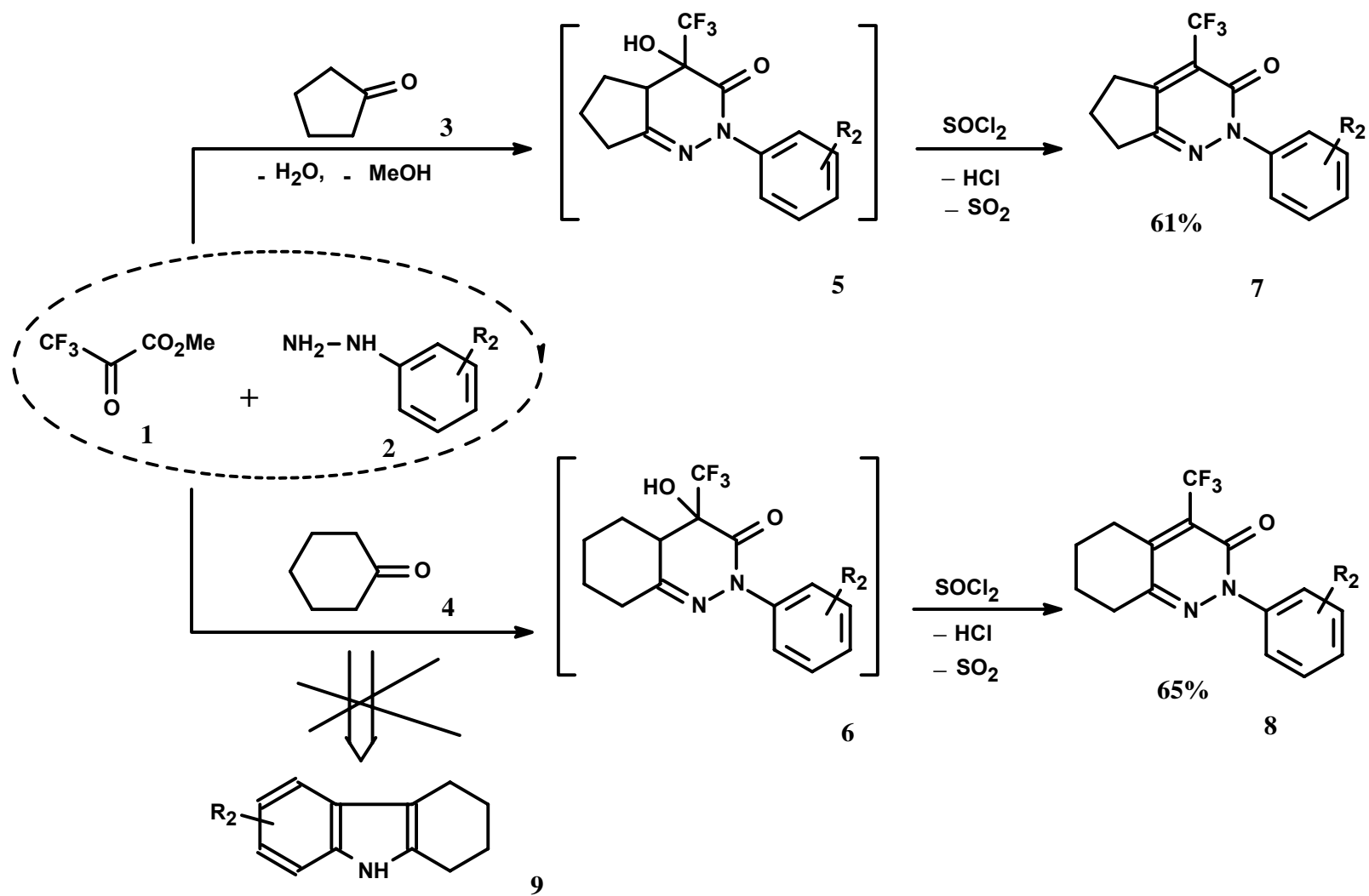
$n$  = 0 - 3

# The mechanism of the novel three-component reaction

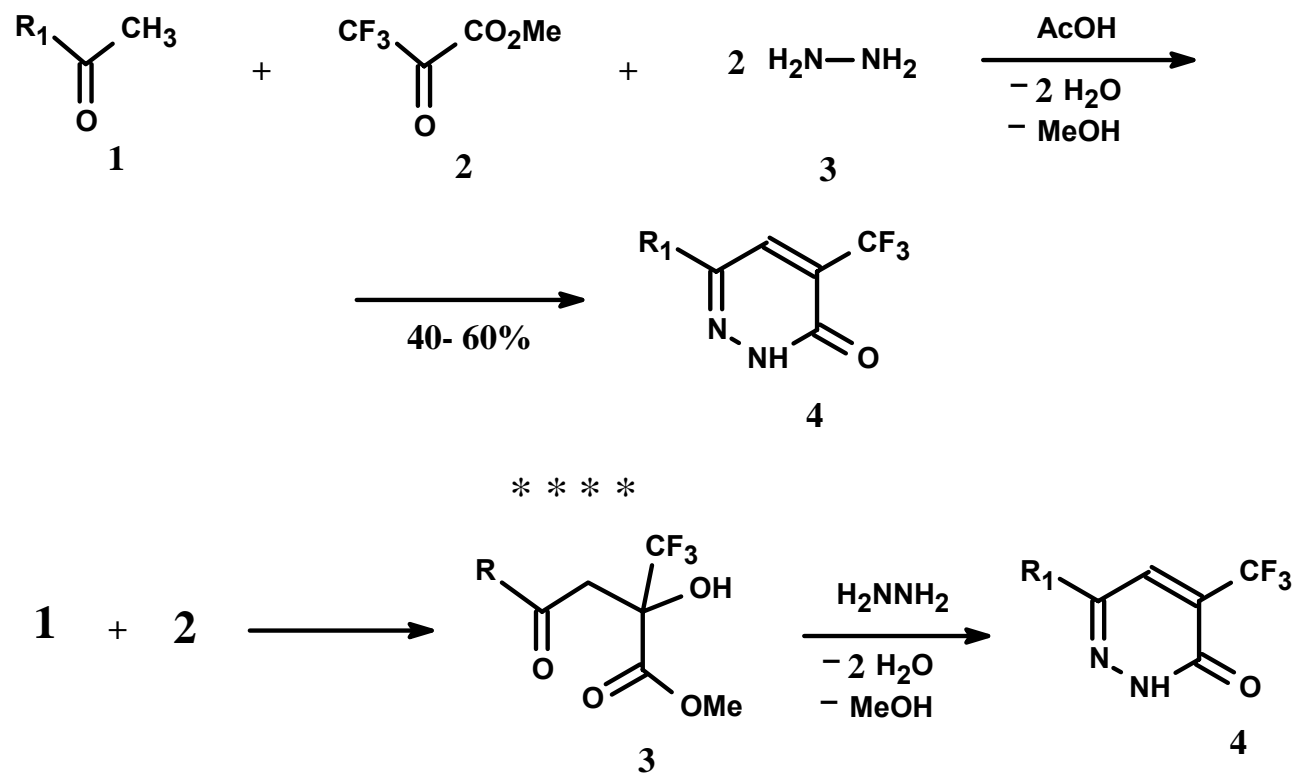




## Reaction with the cyclic ketones

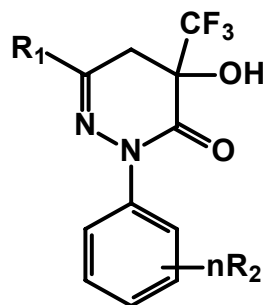


## Hydrazine Hydrate in the Reaction

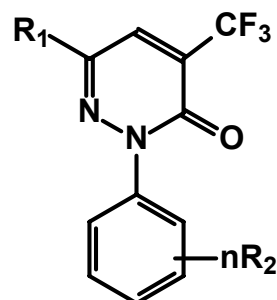


1. Sibgatulin, D.A.; Volochnyuk, D.M.; Kostyuk, A.N.; Syn. Lett.; 12; 2005; 1907 - 1911.

## Insecticide activity 4-Trifluoromethylpiridazin-3-ones



A



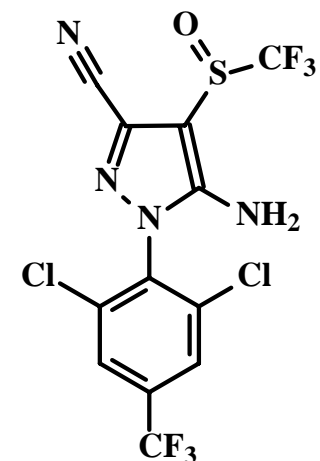
B

$R_1$  = Alk, Ar, Heter

$R_2$  = Me, OMe, Cl, F, Br,  $\text{NO}_2$

$n$  = 0 - 3

One of these compounds has **high insecticide activity**.  
It acts by **blocking the GABA-gated** chloride channels  
of neurons in the central nervous system.



**Flupronil**

- Chipco Choice
- Frontline
- Combat
- Maxforce
- Pereht (BASF)

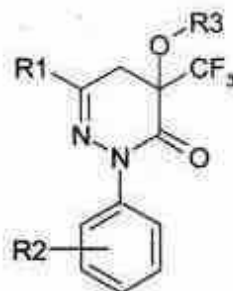
## ISTC1016 PROPOSAL PROJECT (DYACHENKO)

DuPont Contact: Kevin.C.Lee@usa.dupont.com

The project involves the synthesis of the compounds shown below. These compounds were selected from ISTC1016's 07-24-2002 proposal.



1



2

R1 = aryl and heteroaryl are proposed, but we prefer alkyls

R2 = H, Hal, Me, CF<sub>3</sub>, CN

R3 = H, Me

PROJECT ID: IC5-7

Structures 1 thru 3 (please prepare 5-6 examples of each, submit 50 mg)

PREPARATION SCHEME

Please send your synthetic scheme.