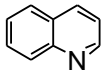


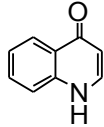
## WYKŁAD 9

### Układy sześcioczłonowe

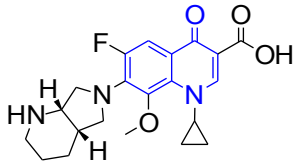
#### 1. Pochodne chinolonu - moksifloksacyna (INN, *moxifloxacin*)



**Chinolina**

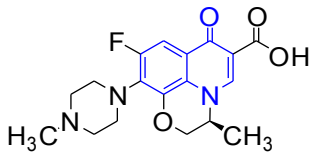


**1H-Chinolin-4-on  
(Chinolon)**



**Moksifloksacyna  
(INN, moxifloxacin)**

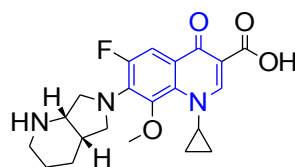
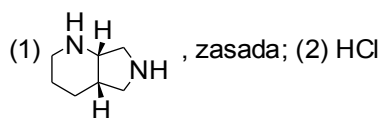
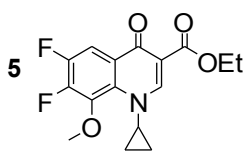
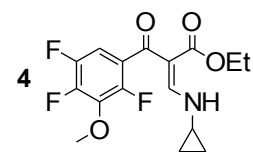
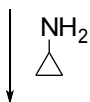
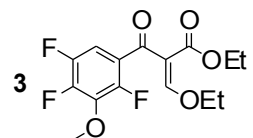
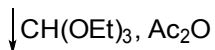
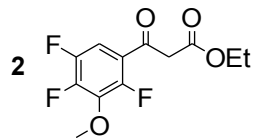
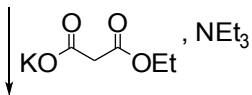
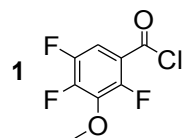
Antybiotyki o szerokim spektrum działania, aktywne przeciwko bakteriom Gram-dodatnim, Gram-ujemnym i beztlenowym. Stosowane m.in. w infekcjach górnych i dolnych dróg oddechowych, układu pokarmowego lub moczowego.



**Lewofloksacyna  
(INN, levofloxacin)**

## Sekwencja Grohe-Heitzera syntezy 3-karboksychinolonów (1 – 5)

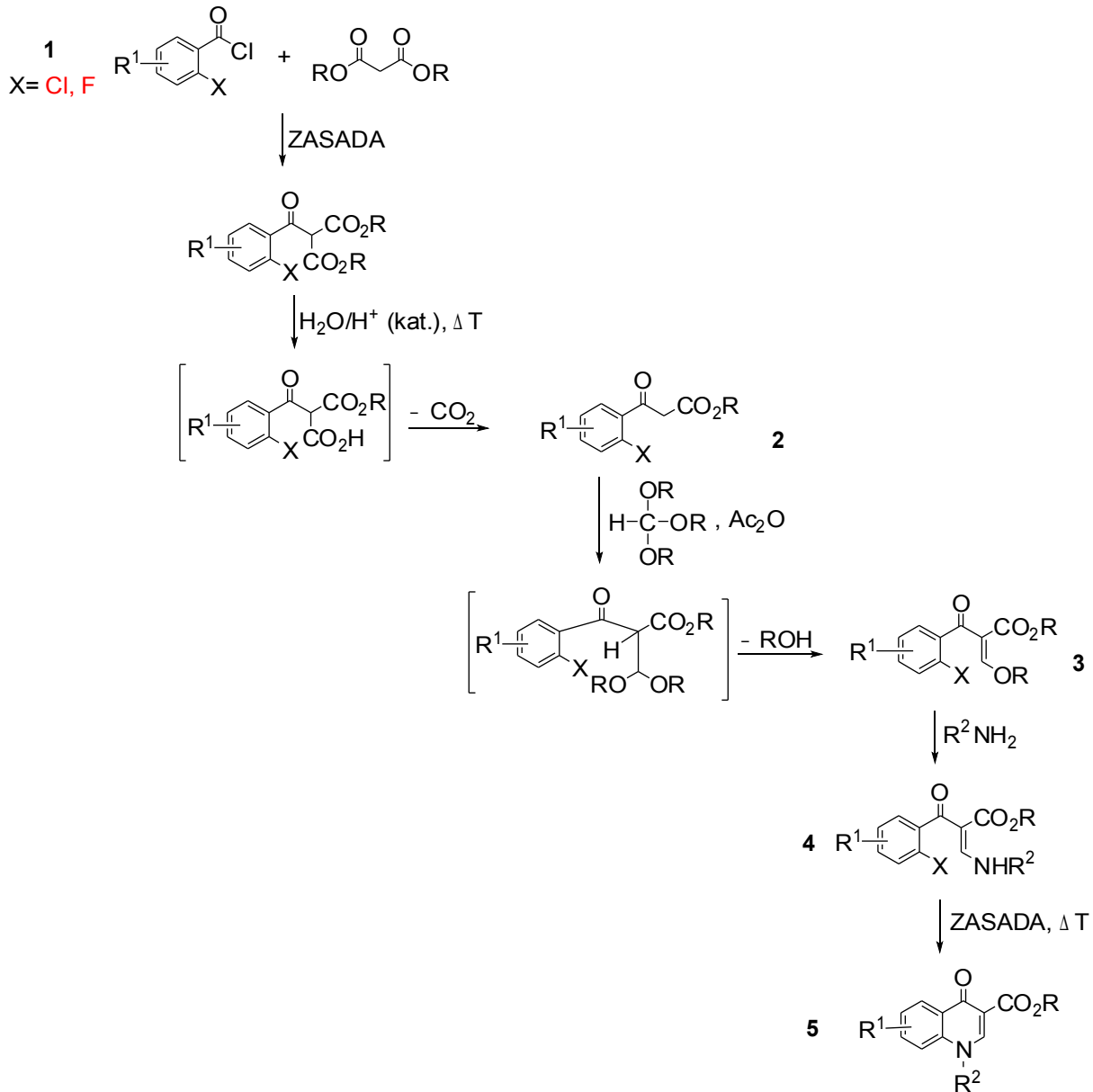
*Recent Pat. Anti-infect. Drug Discovery, 2006, 1, 33.*  
*J. Labelled Cpd. Radiopharm. 2000, 43, 795.*  
*Drugs Fut. 1997, 109.*



**Moksifloksacyna**

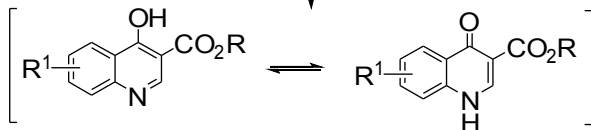
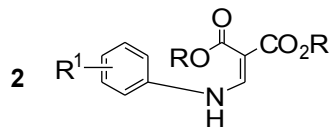
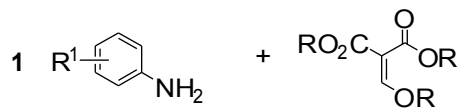
## 1.2. Wyjaśnienie przebiegu wybranych etapów

### 1.2.A. Sekwencja Grohe-Heitzera syntezy 3-karboksychinolonów

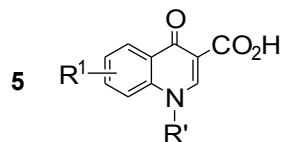
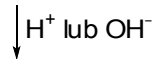
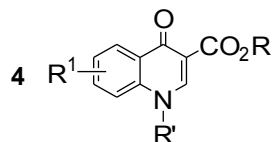
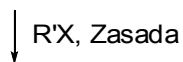


## 1.2.B. Sekwencja Goulda-Jacobsa syntezy 3-karboksychinolonów

*Curr. Med. Chem.* 2003, 10, 21.

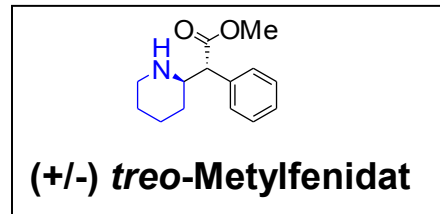


3

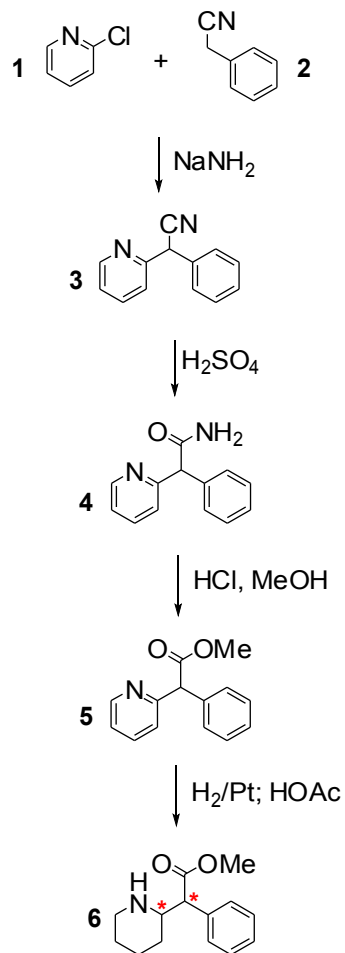


## 2. Pochodne piperyny - metylfenidat (INN, *methylphenidate*)

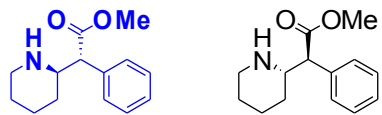
Zarejestrowany w 1958 r. jako Ritalin® do leczenia przemęczenia, nudności i depresji, a od 1960 r. stosowany w leczeniu nadpobudliwości (ADHD) u dzieci.



### 2.1. Synteza racematu

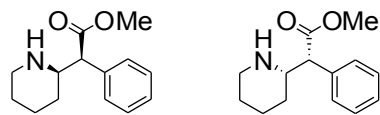


(+/-) treo



Aktywny

(+/-) erytro



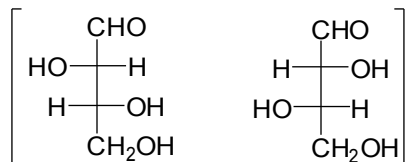
(+/-) treo : (+/-) erytro  
20 : 80

*Helv. Chim. Acta* 1944, 27, 1748.

### Konfiguracja erytro (lub treo)

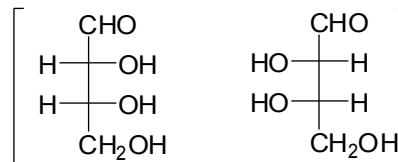
- zwyczajowe określenie konfiguracji względnej przez analogię do erytrozy (lub treozy)

Ta konwencja nie ma związku z konfiguracją absolutną na centrach asymetrii w rozpatrywanej pochodnej.



D-treozja

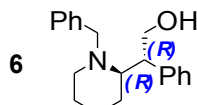
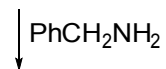
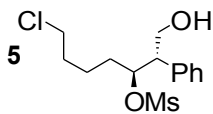
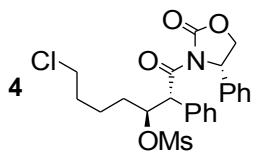
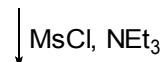
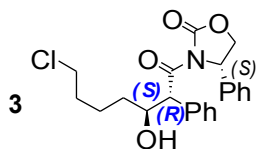
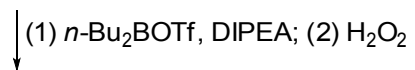
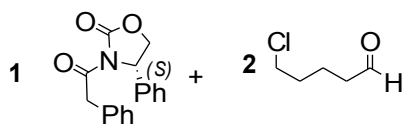
L-treozja

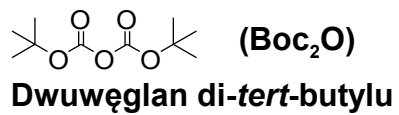
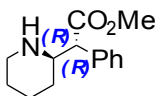
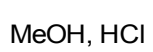
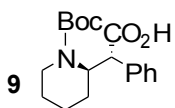
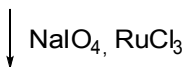
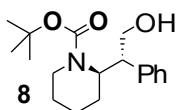
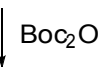
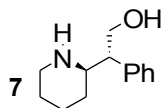
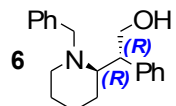


D-erytrozja

L-erytrozja

## 2.2. Synteza asymetryczna (*R,R*)-metylfenidatu



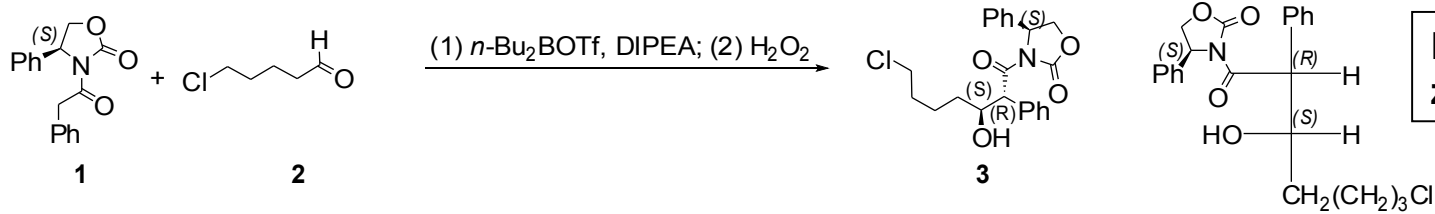


*J. Am. Chem. Soc.* 1981, 103, 2127.  
*J. Am. Chem. Soc.* 1982, 104, 1737.

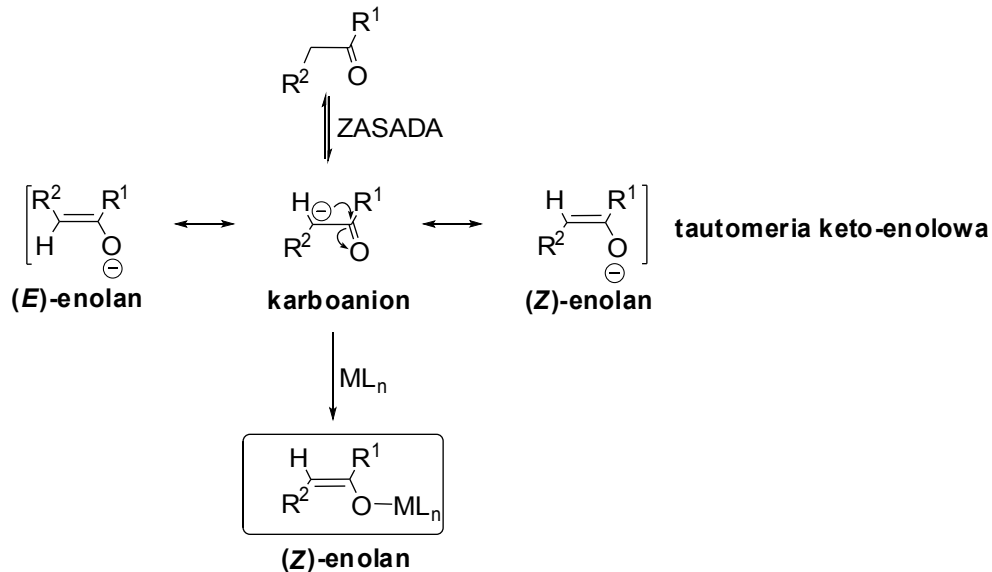
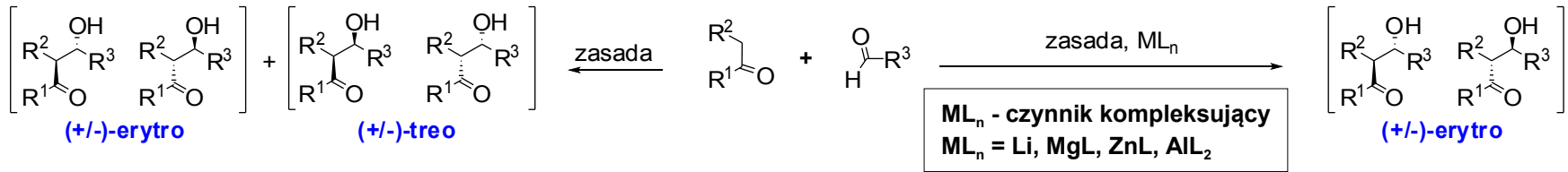


## 2.2.1. Wyjaśnienie przebiegu wybranych etapów

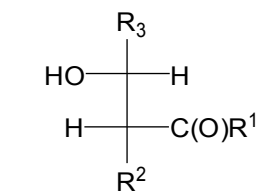
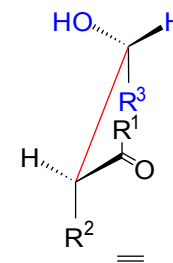
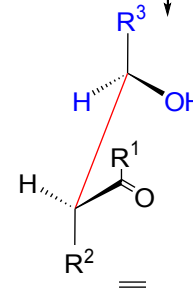
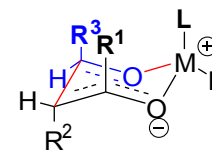
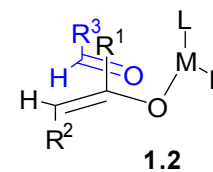
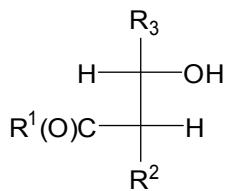
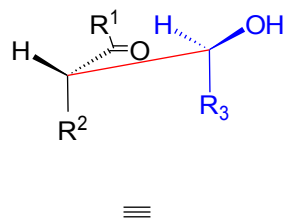
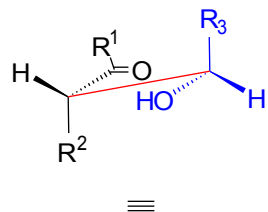
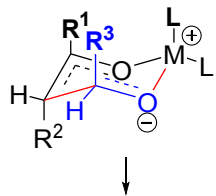
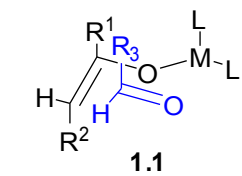
### Erytro-selektywna kondensacja aldolowa z udziałem enolanu boru



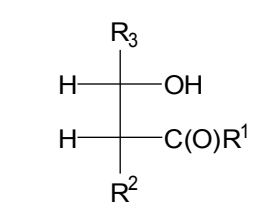
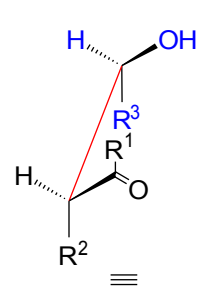
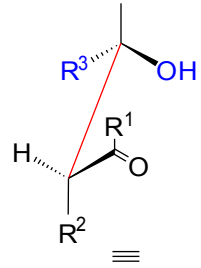
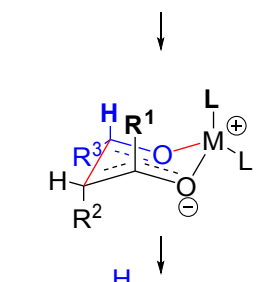
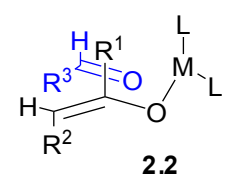
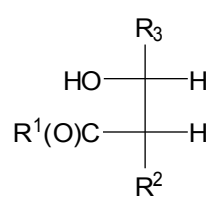
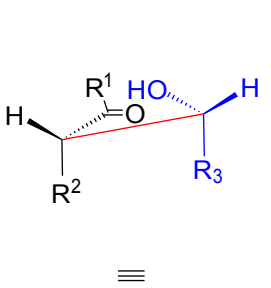
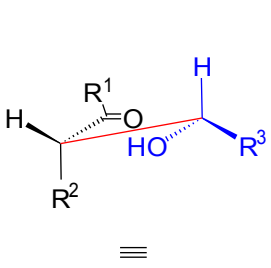
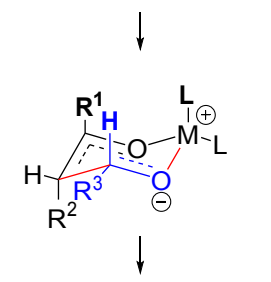
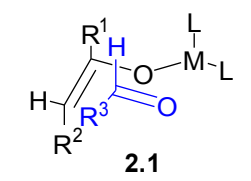
Konfiguracja erytro  
zw. 3 ze slajdu 7



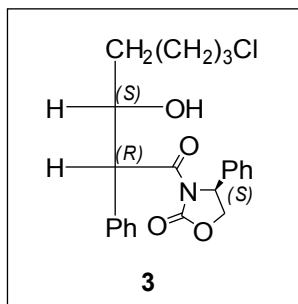
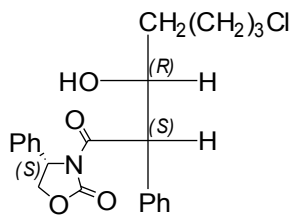
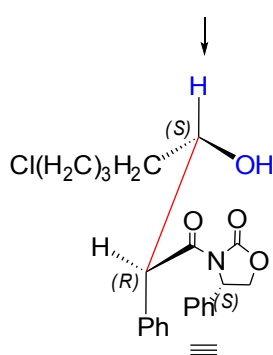
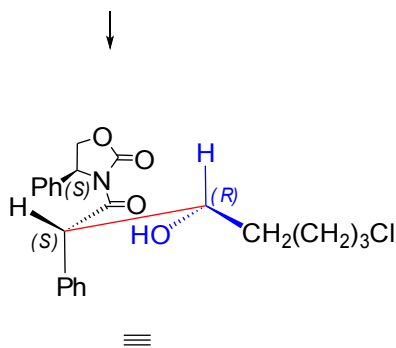
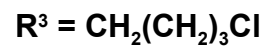
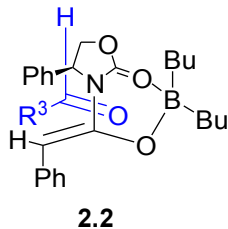
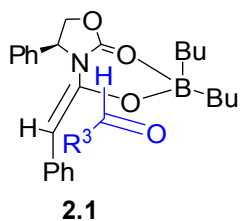
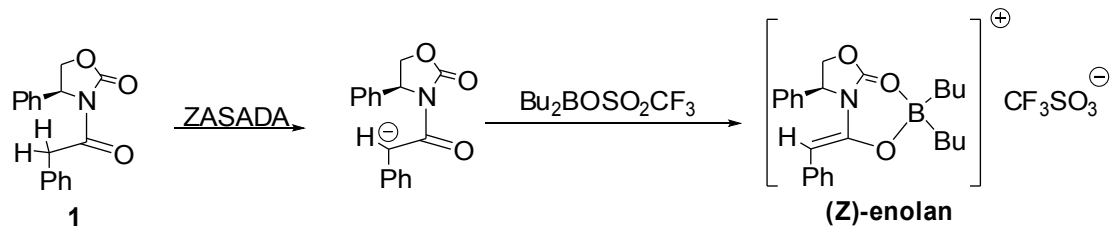
WARIANT 1



**WARIANT 2**



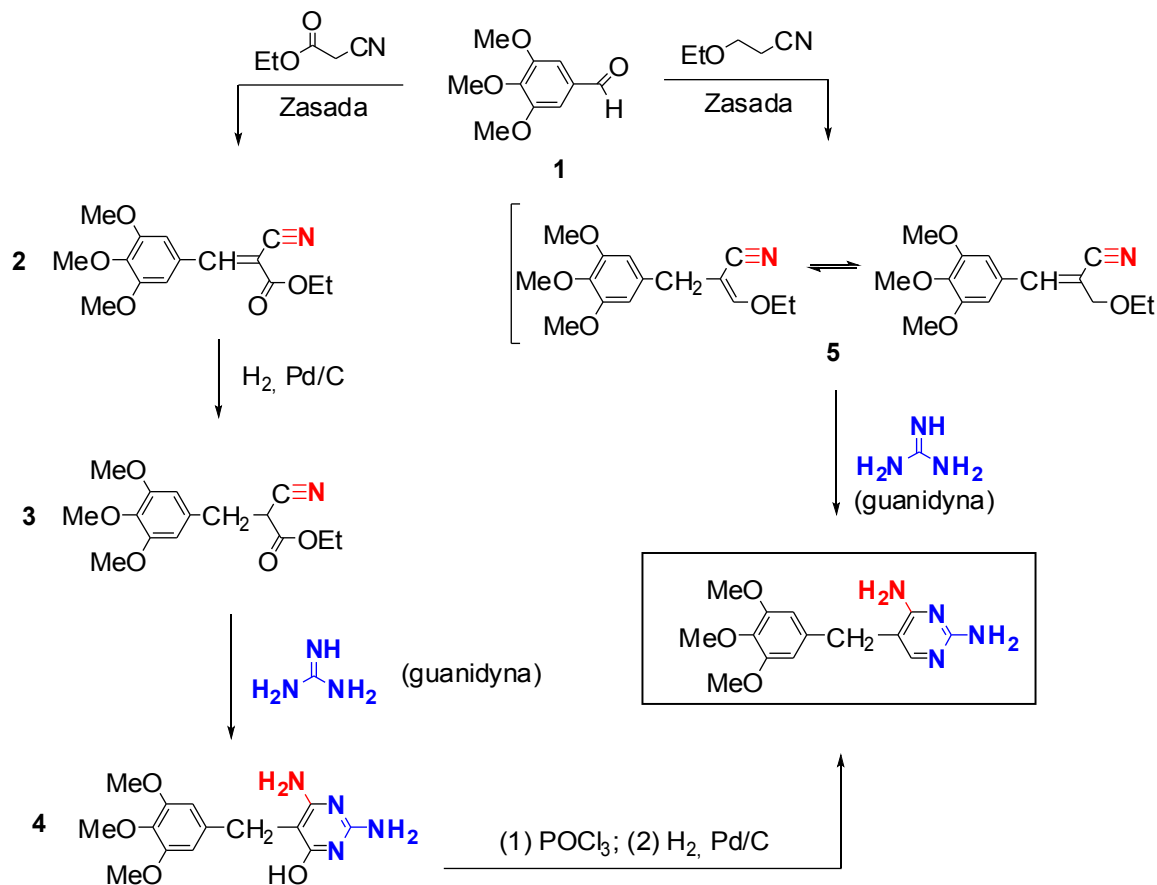
# Przebieg syntezy zw. 3 zgodnie z wariantem 2.



### 3. Pochodne pirymidyny - trymetoprym (INN, *trimethoprim*)

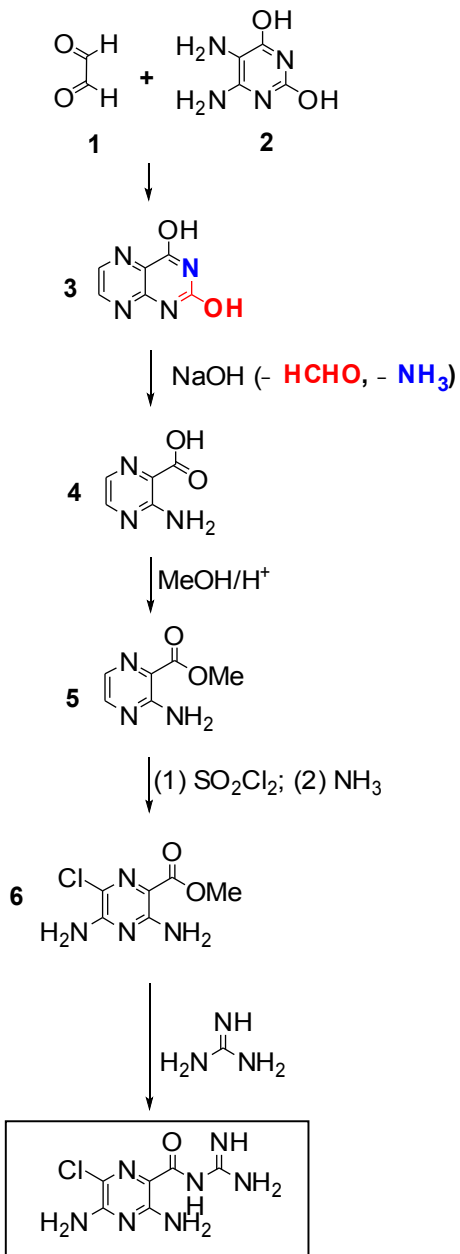
Lek o działaniu przeciwbakteryjnym i przeciwmalarycznym

Ger. Pat. 1.445.176 (1960).  
US Pat. 3.049.544 (1962).  
Ger. Pat. 1.795.586 (1974).  
Ger. Pat. 2.635.765 (1978).



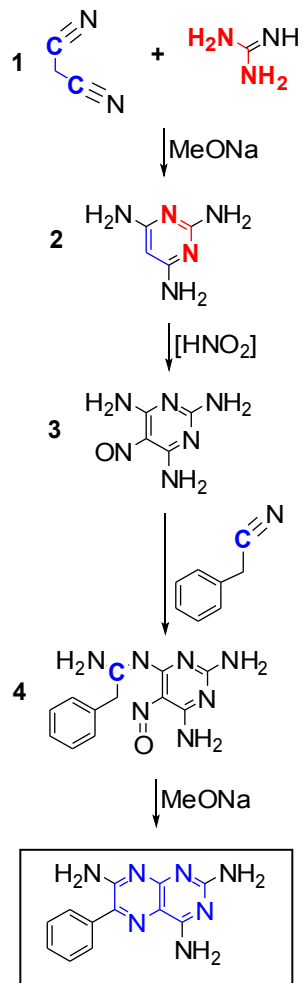
Ger. Pat. 2.165.362 (1970).  
Ger. Pat. 2.258.238 (1971).

#### 4. Pochodne pirazyny - amilorid (INN, *amiloride*) Diuretyk (lek moczopędny), stosowany w celu obniżenia ciśnienia krwi.

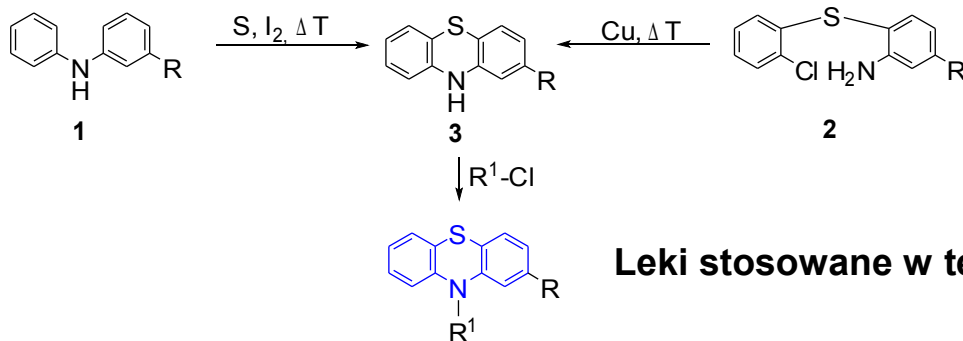


## 5. Pochodne pterydyny - triamteren (INN, *triamterene*)

Diuretyk stosowany w terapii chorób krążeniowych



## 6. Pochodne fenotiazyny - promazyna i jej analogi (INN, *promazine*)



Leki stosowane w terapii chorób psychicznych

Nazwa preparatu	R	R <sup>1</sup>
Promazyna ( <i>promazine</i> )	H	
Chlorpromazyna ( <i>chlorpromazine</i> )	Cl	
Metopromazyna ( <i>methopromazine</i> )	OCH <sub>3</sub>	-CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -N(CH <sub>3</sub> ) <sub>2</sub>
Triflupromazyna ( <i>triflupromazine</i> )	CF <sub>3</sub>	
Acepromazyna ( <i>acepromazine</i> )	C(O)CH <sub>3</sub>	
Trimeprazyna ( <i>trimeprazine</i> )	H	
Lewomepromazyna ( <i>methotrimeprazine</i> )	OCH <sub>3</sub>	-CH <sub>2</sub> -CH(CH <sub>3</sub> )-CH <sub>2</sub> -N(CH <sub>3</sub> ) <sub>2</sub>
Metiomeprazyna ( <i>methiomeprazine</i> )	SCH <sub>3</sub>	