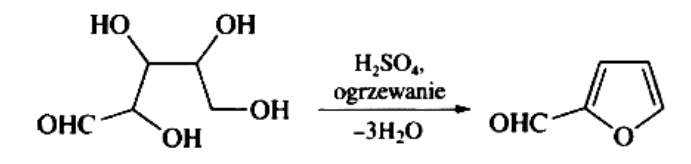
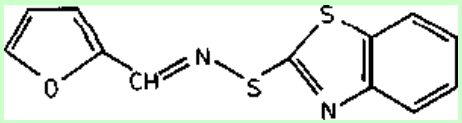
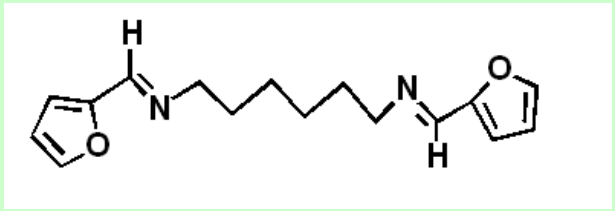
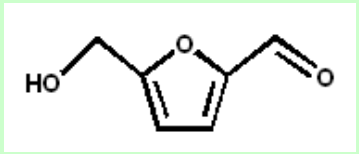
PIĘCIOCZŁONOWE PIERŚCIENIE HETEROAROMATYCZNE Z JEDNYM HETEROATOMEM

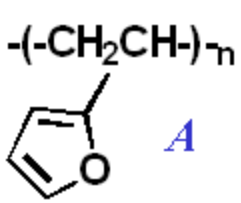
Znaczenie pirolu, furanu, tiofenu i ich pochodnych

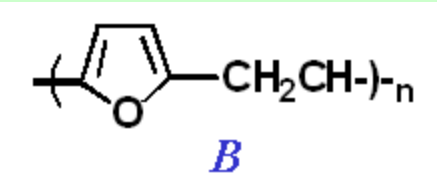


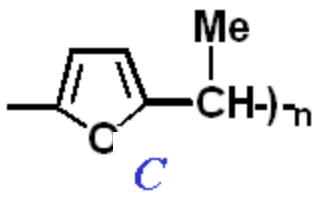


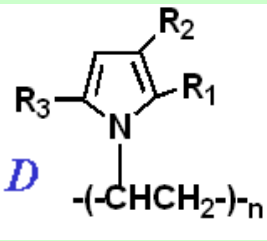


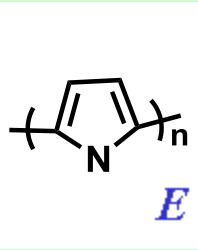


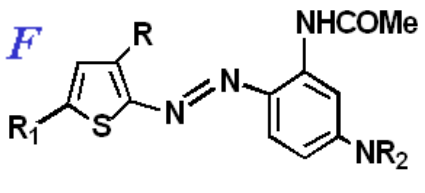

-(-CH2CH-)-n
A

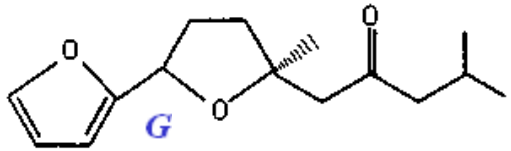

CH2CH-)-n
B

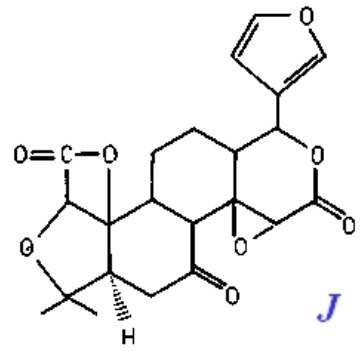

Me
CH-)-n
C

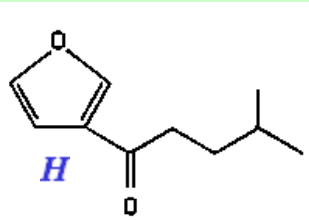

R2
R3
R1
N
D
-(-CHCH2-)-n

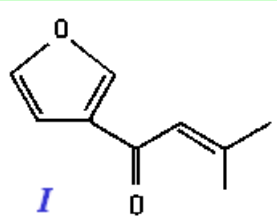

n
N
E

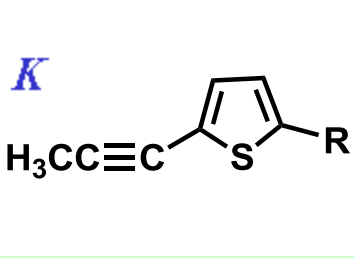

F
R
NHCOMe
R1
S
N
N
NR2

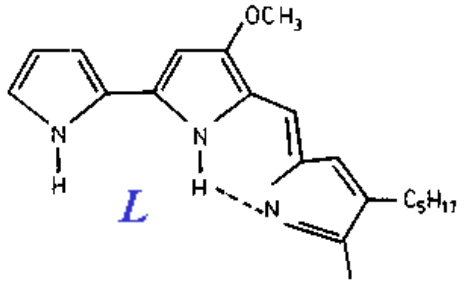

O
O
O
G

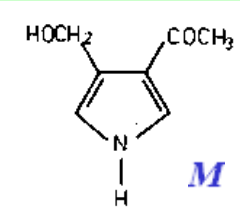

O
O=C-O
O
O
O
O
O
H
J

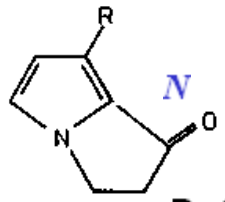

O
H
O


O
I
O

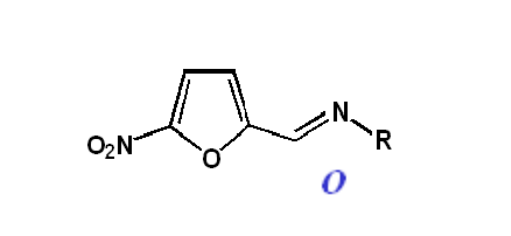

K
H3CC≡C
S
R


OCH3
N
H
N
H
N
C5H11
L

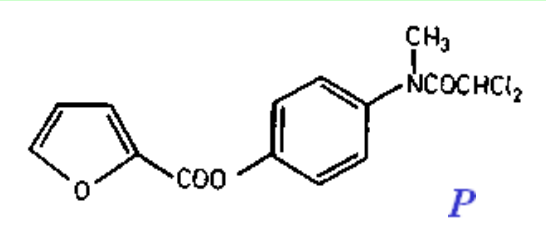

HOCH2
COCH3
N
H
M


R
N
O
N

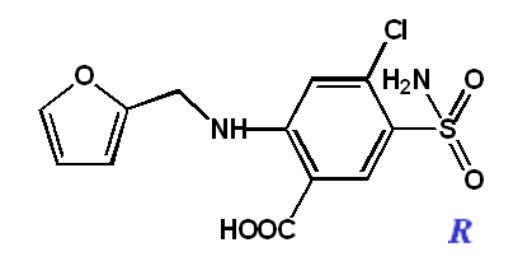
R= CH_3,CHO



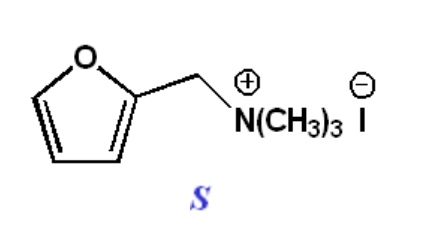
O



P

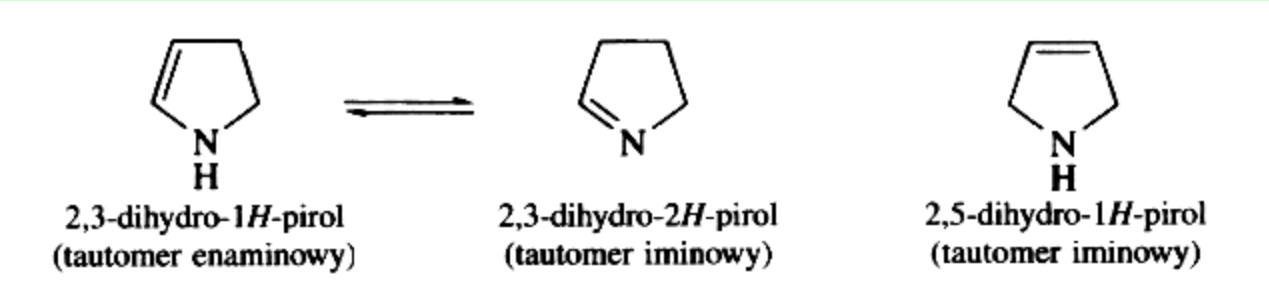


R



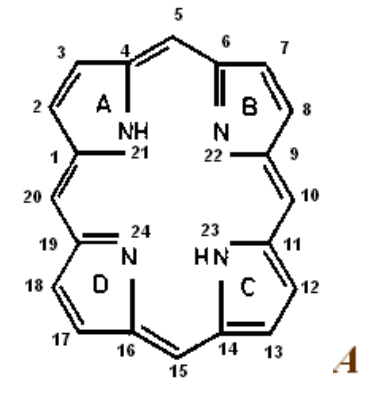
S

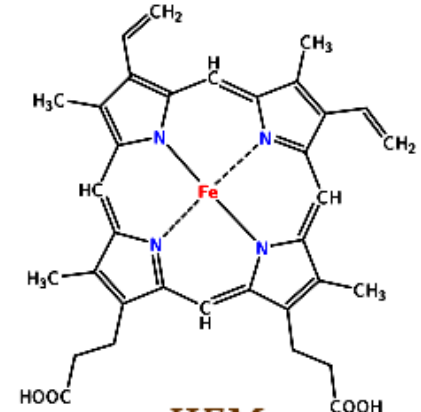
•Formy częściowo uwodornione to trzy dihydropirole , z których mniej trwały jest 2,5-dihydro-1*H*-pirol (3-pirolina).

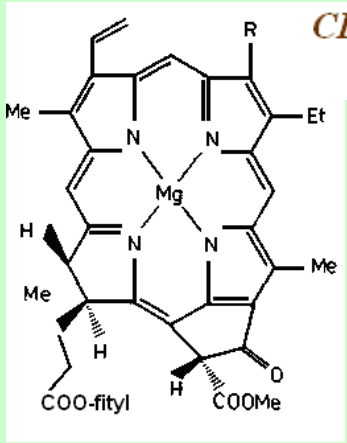


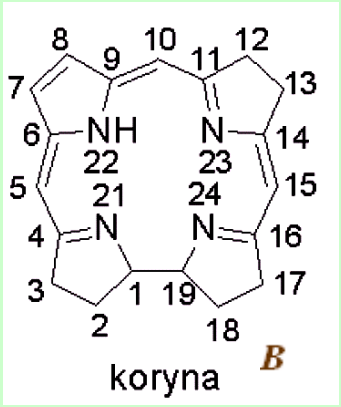
2,3-dihydro-1*H*-pirol (tautomer enaminowy) ⇌ 2,3-dihydro-2*H*-pirol (tautomer iminowy)

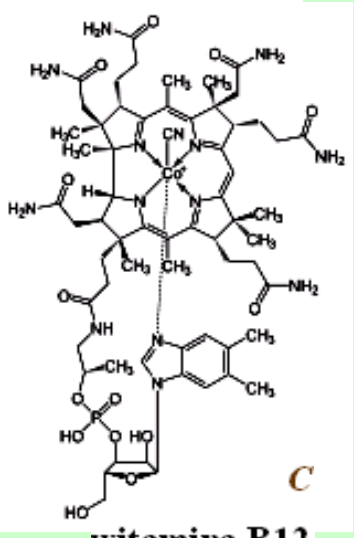
2,5-dihydro-1*H*-pirol (tautomer iminowy)

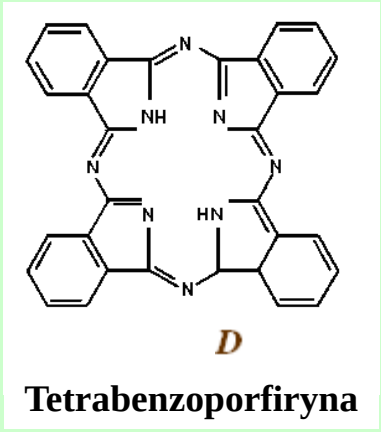

A
NH
N
N
HN
D
C
B

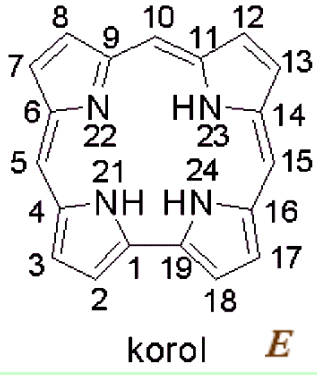

Fe
HEM

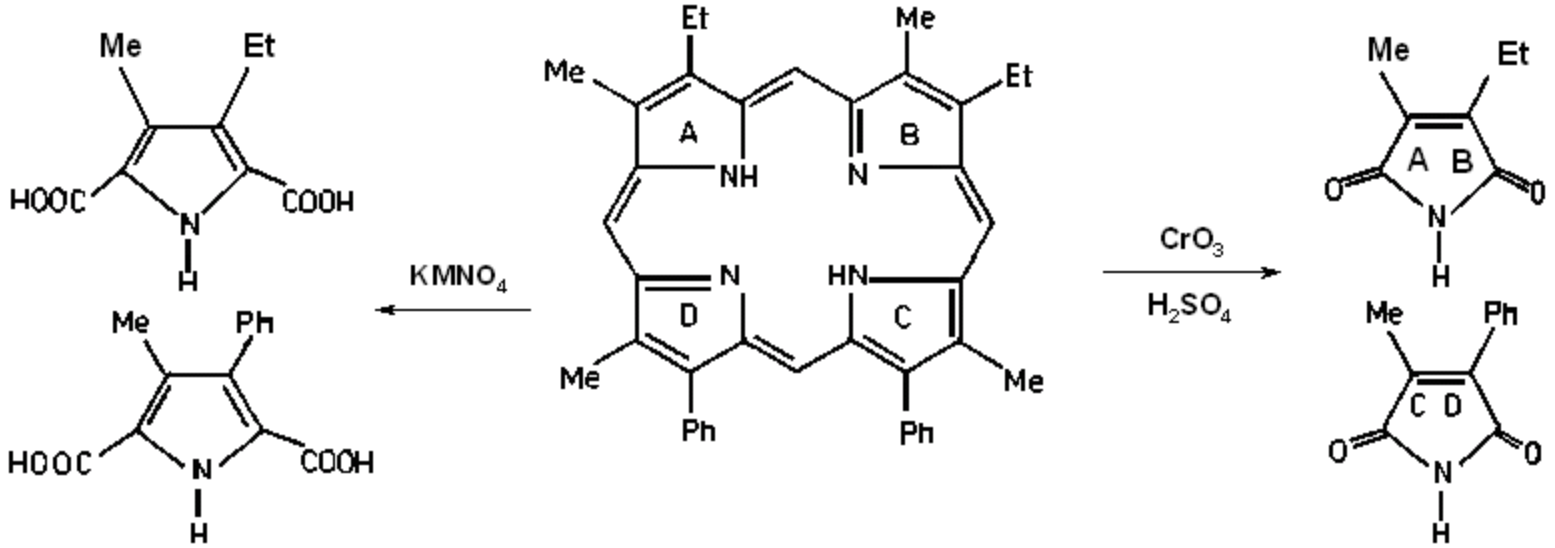

CHLOROFIL A R=Me
B R =CHO
Mg
COO-fityl
COOMe

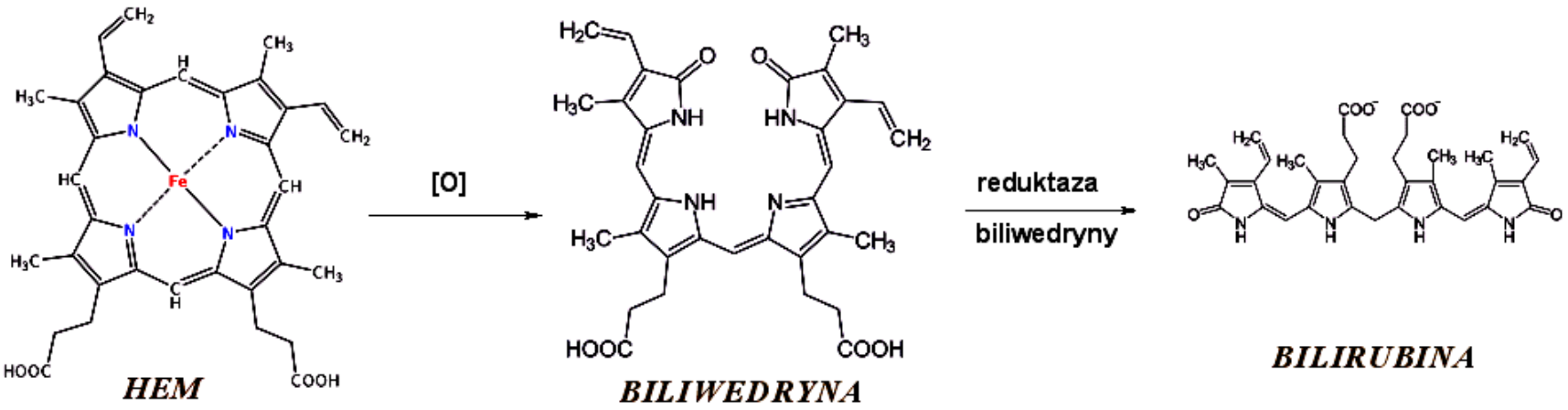

koryna
B

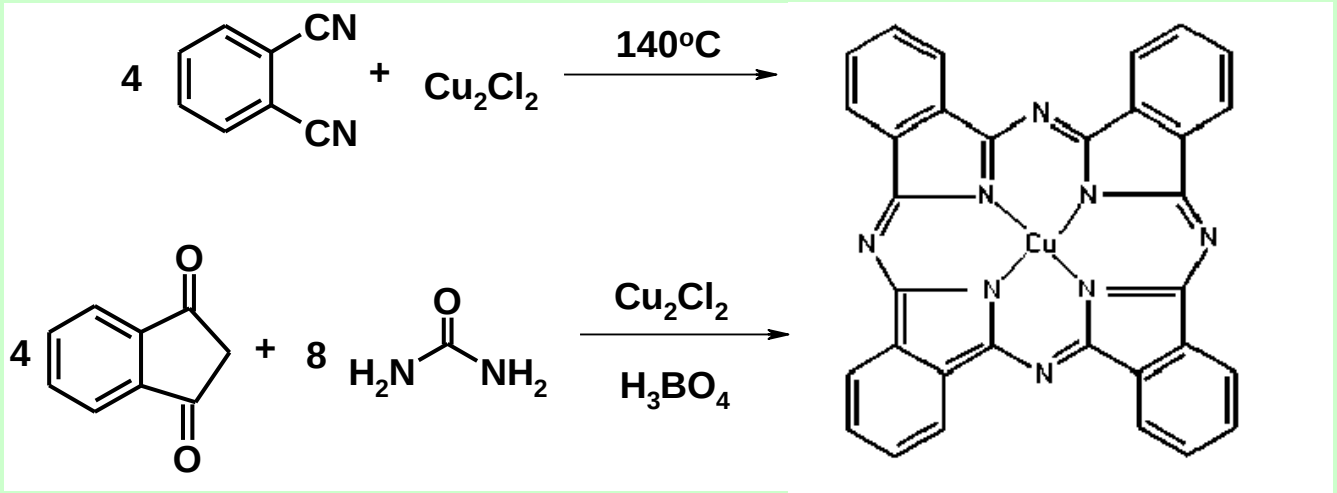

C
witamina B12


D
Tetrabenzoporfiryna


korol
E

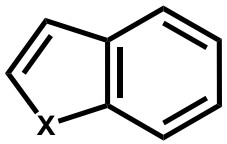

Me
Et
HOOC
COOH
N
H
Me
Ph
HOOC
COOH
N
H
KMNO4
Et
Me
Me
Et
A
B
NH
N
N
HN
D
C
Me
Me
Ph
Ph
CrO3
H2SO4
Me
Et
A B
O
O
N
H
Me
Ph
C D
O
O
N
H

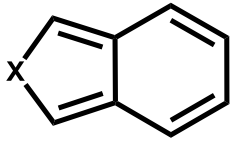

HEM
[O]
BILIWEDRYNA
reduktaza
biliwedryny
BILIRUBINA

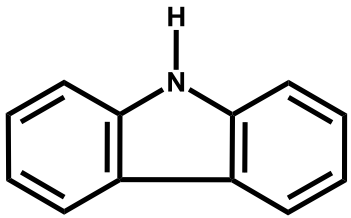

4
CN
CN
+
Cu2Cl2
140°C
4
+
8
H2N
NH2
Cu2Cl2
H3BO4
Cu

BENZOLOGI PIROLU, FURANU l TIOFENU

Struktura benzologów pirolu, furanu i tiofenu







X= NH, O, S

benzo[*b*]pirol X= NH
(indol)

benzo[*b*]furan X= O
(benzofuran)

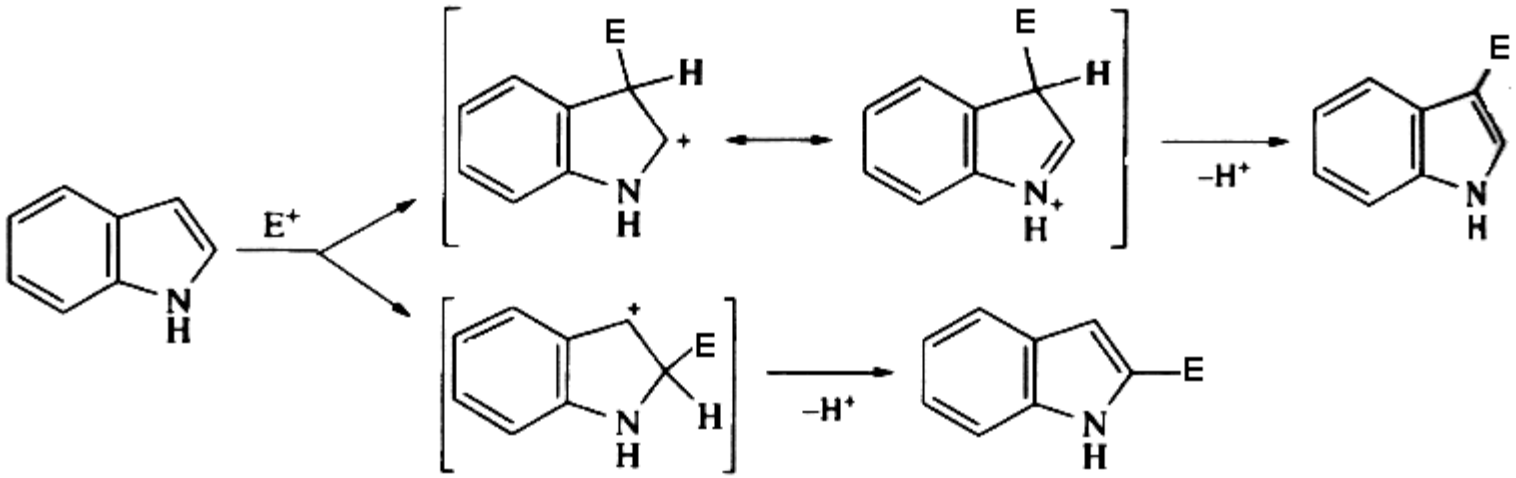
benzo[*b*]tiofen X= S
(tionaften)

benzo[*c*]pirol X= NH
(izoindol)

benzo[*c*]furan X= O
(izobenzofuran)

benzo[*c*]tiofen X= S
(izobenzotiofen)

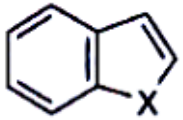
karbazol


E+
E
H
N
H
–H+
E
H
N
H
E
N
H
–H+
E
N
H
E

Widma IR, UV i NMR – charakterystyczne cechy ułatwiające określanie struktury benzologów pirolu, furanu i tiofenu

- **W widmach elektronowych benzopirolu, benzofuranu i benzotiofenu obserwuje się strukturę trójpasmową, podobnie jak w izoelektronowym z nimi naftalenie.**
- **W stosunku do ich jednopierścieniowych analogów obserwuje się batochromowe przesunięcie pasm absorpcji.**

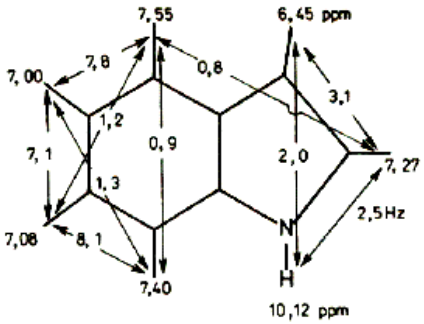
UV widma[nm] benzo[b]heterocykli (w heptanie), i benzo[c]heterocykli (w heksanie)

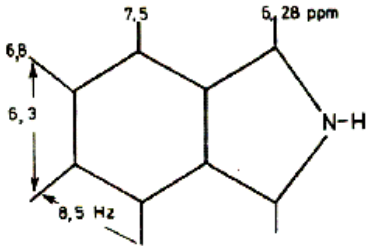


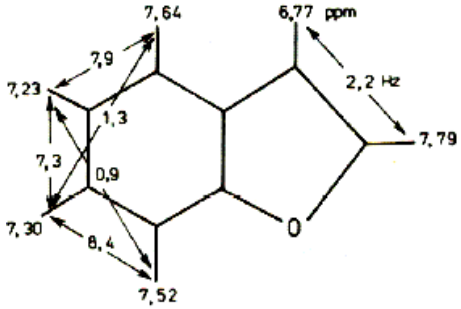
Compound	λ_{max} *(log ε)*						
Indole	215 (4.38)	261 (3.69)	266.5 (3.70)	277sh (3.58)	279 (3.62)	287 (3.51)	–
Benzofuran	–	239.5 (4.03)	240.5 (4.03)	244.5 (4.04)	250.5 (3.91)	269 (3.23)	271 (3.25)
						275 (3.40)	281 (3.49)
Benzothiophene	228 (4.45)	263sh (3.71)	258 (3.76)	281 (3.19)	288.5 (3.33)	290.5 (3.33)	297 (3.52)
Benzoselenophene	236 (4.45)	260 (3.70)	270sh (3.52)	296 (3.56)	298 (3.54)	305 (3.79)	–
Benzotellurophene	214 (4.43)	251 (4.43)	–	312sh (4.15)	318 (4.2)	–	–

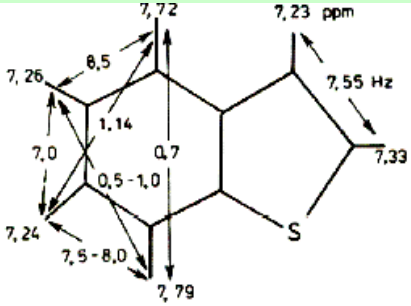
Compound	λ_{max} *(log ε)*
Benzo[*c*]indole	263.5, 268.5, 275, 286.5, 294sh, 300, 306.5, 312.5, 320, 326.5, 335
Benzo[*c*]furan	215 (4.17), 244 (3.4), 249 (3.37), 254 (3.35), 261 (3.12), 292sh (3.35), 299sh (3.47), 305sh (3.56), 313 (3.7), 319 (3.7), 327 (3.87), 334 (3.66), 343 (3.79)
Benzo[*c*]thiophene	215 (4.84) 257sh (4.04), 272 (3.94), 278 (3.94), 283sh (3.93), 290 (3.97), 295 (3.96), 298sh (3.94), 305 (4.06), 313 (3.89), 318 (3.90), 322 (3.88), 328 (3.91), 333 (3.90), 343 (3.79)
Benzo[*c*]selenophene	273, 286, 291, 298, 302sh, 305sh, 312, 323, 328, 336sh, 340, 344sh, 353, 357, 362sh

•Widma ^{1}H i ^{13}C i ^{15}N NMR rozważanych związków mają duże znaczenie dla określania położenia podstawników.

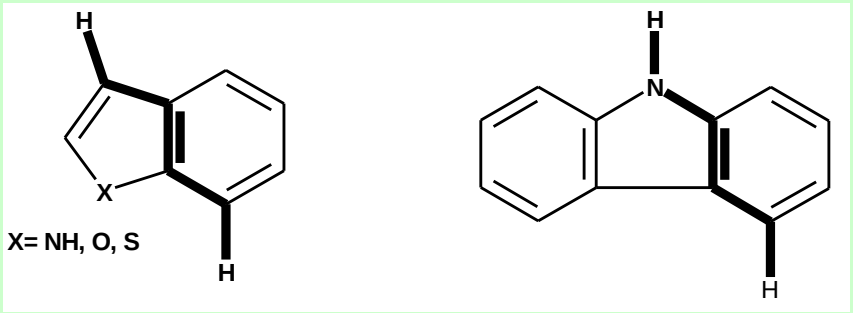


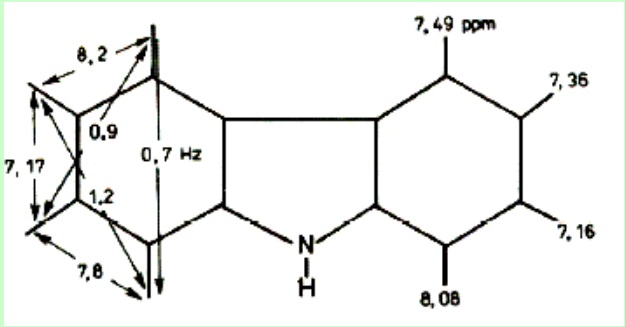




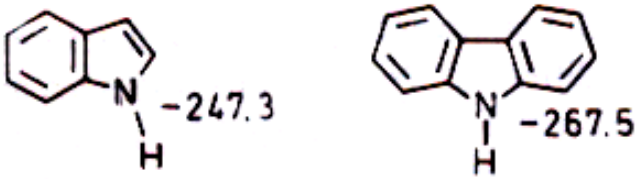


^{1}H

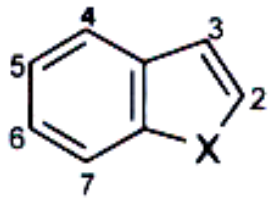




^{15}N



^{13}C



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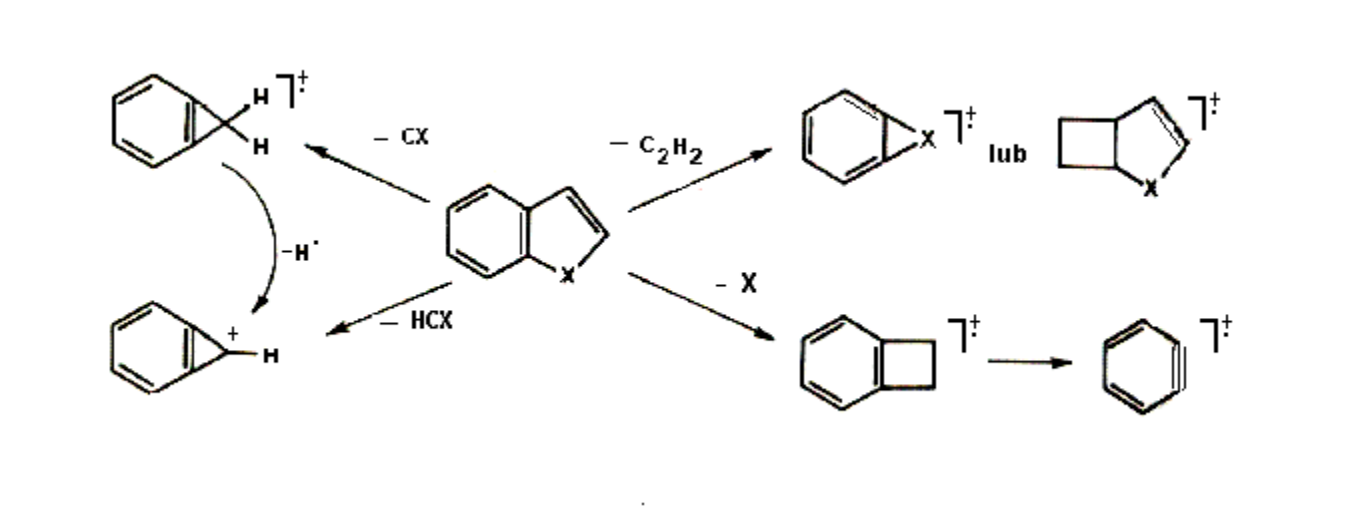
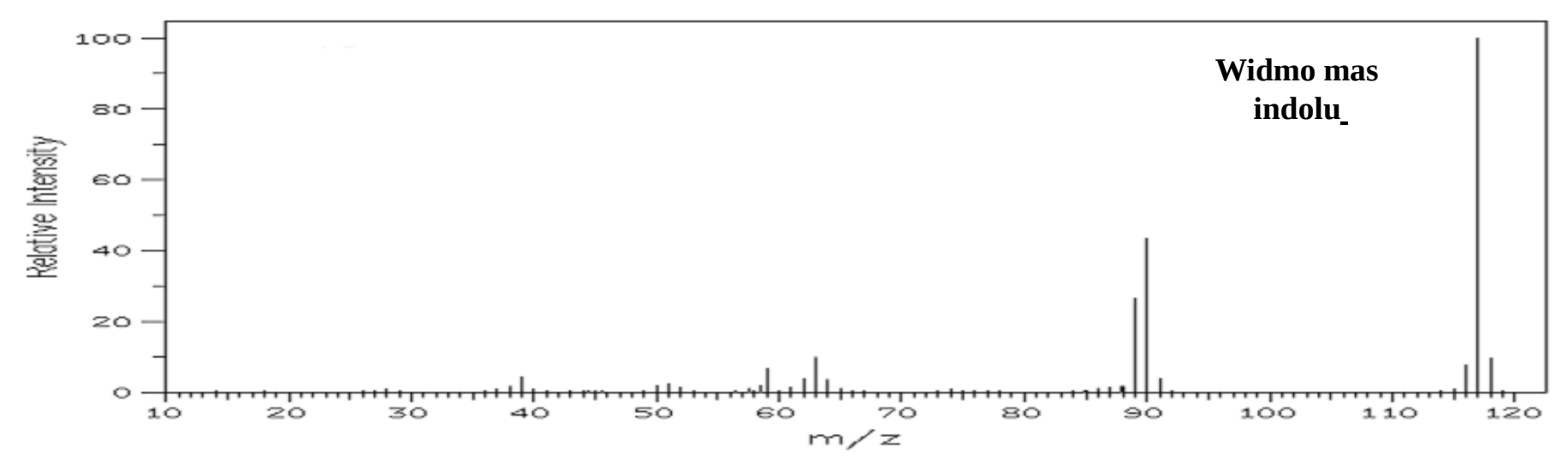
	Iindol	*Benzofuran*	*Benzotiofen*
C(2)	124.67	145.1	126.21
C(3)	102.14	106.9	123.79
C(4)	120.76	121.6	123.57
C(5)	121.81	123.2	124.10
C(6)	119.76	124.6	124.17
C(7)	111.35	111.8	122.44
C(7a)	135.65	155.5	139.71
C(3a)	128.26	127.9	139.57
Rozpuszczalnik	dioksan	CS_2	$CDCl_3$

•**Widma mas**

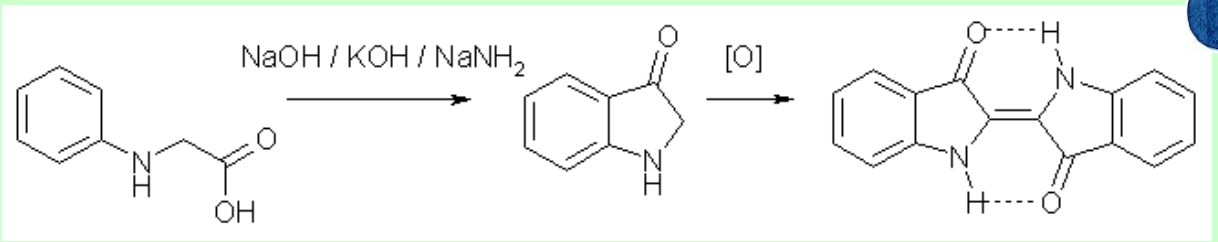
•**Udział poszczególnych kationorodników w widmie jest różny w zależności od heteroatomu.**

- indol i jego pochodne ulegają fragmentacji w stosunkowo niewielkim stopniu, głównie utrata HCN i H_2CN- intensywne sygały *m/e* 90 (40%) i 89 (24%).



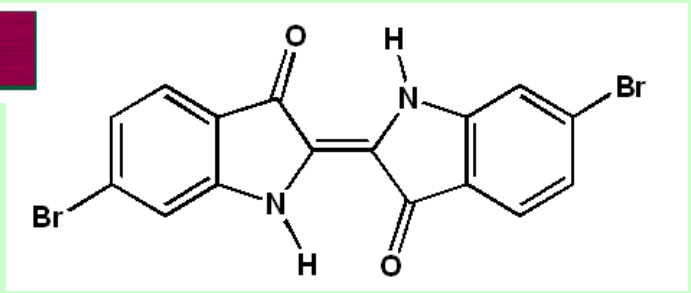


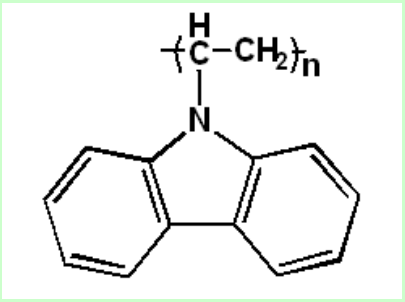
Zastosowanie i znaczenie biologiczne benzologów pirolu, furanu i tiofenu



indygo

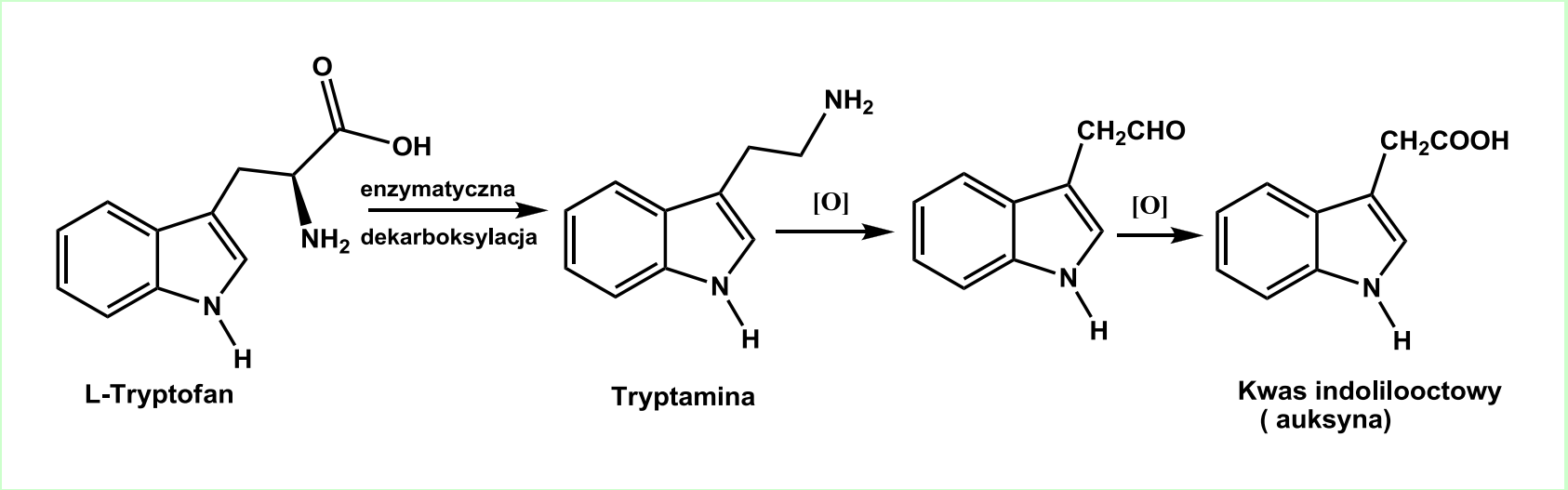
Metoda Pflegera syntezy indygo



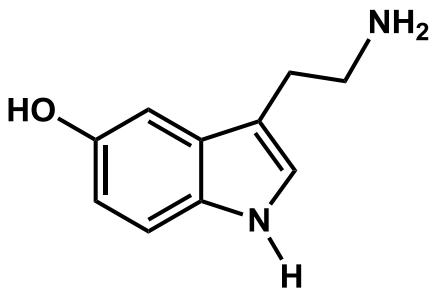


purpura tyryjska (purpura antyczna lub starożytna).

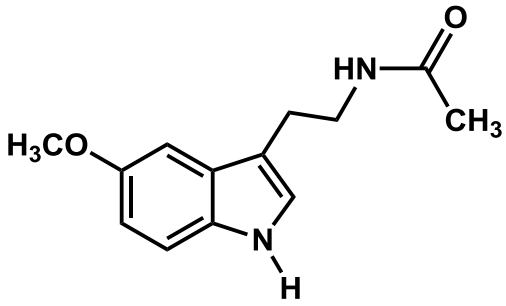
Luvican



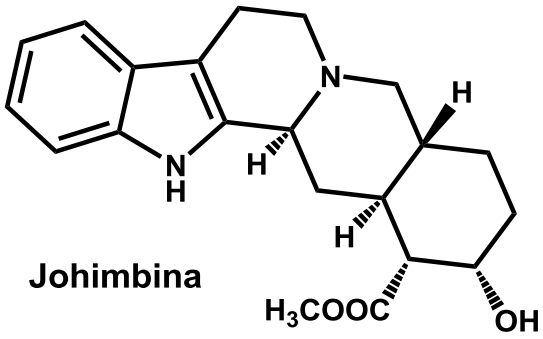
Zastosowanie i znaczenie biologiczne benzologów pirolu, furanu i tiofenu



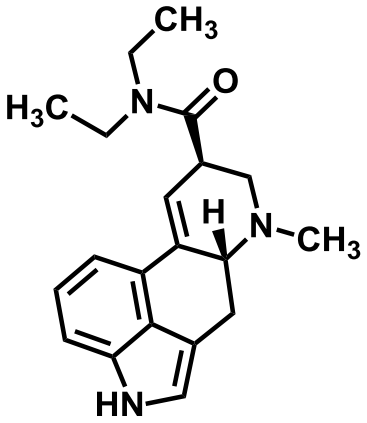
Serotonina (5-hydroksytryptamina)



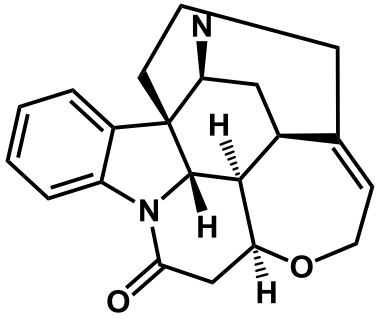
Melatonina (N-acetylo-5-metoksytryptamina)



Johimbina



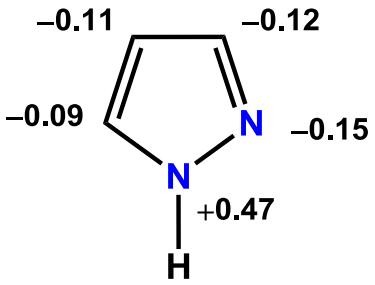
LSD (Dietyloamid kwasu D-lizergowego)



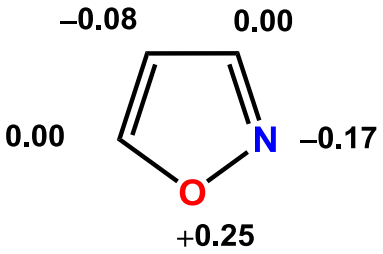
Strychnina

PIĘCIOCZŁONOWE PIERŚCIENIE HETEROAROMATYCZNE Z DWOMA i WIĘKSZĄ LICZBĄ HETEROATOMÓW

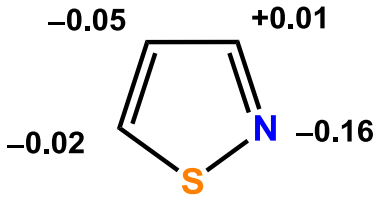
1. Azole



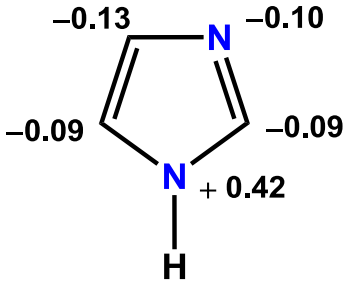
pirazol



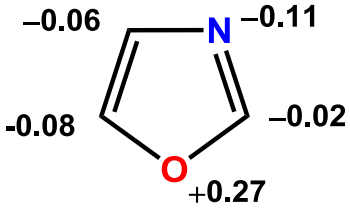
izoksazol



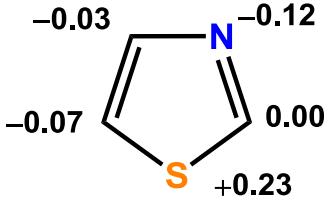
izotiazol



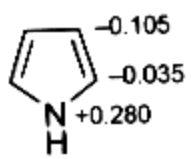
Imidazol

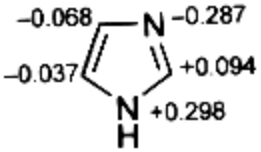


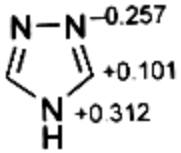
oksazol

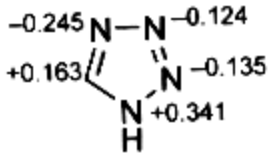


tiazol

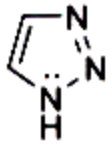




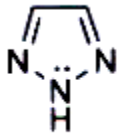




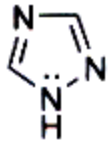
4*H*-1,2,3-triazol **1*H*-tetrazol**



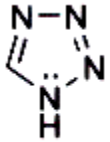
1*H*-1,2,3-triazol



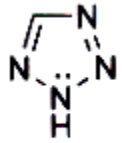
2*H*-1,2,3-triazol



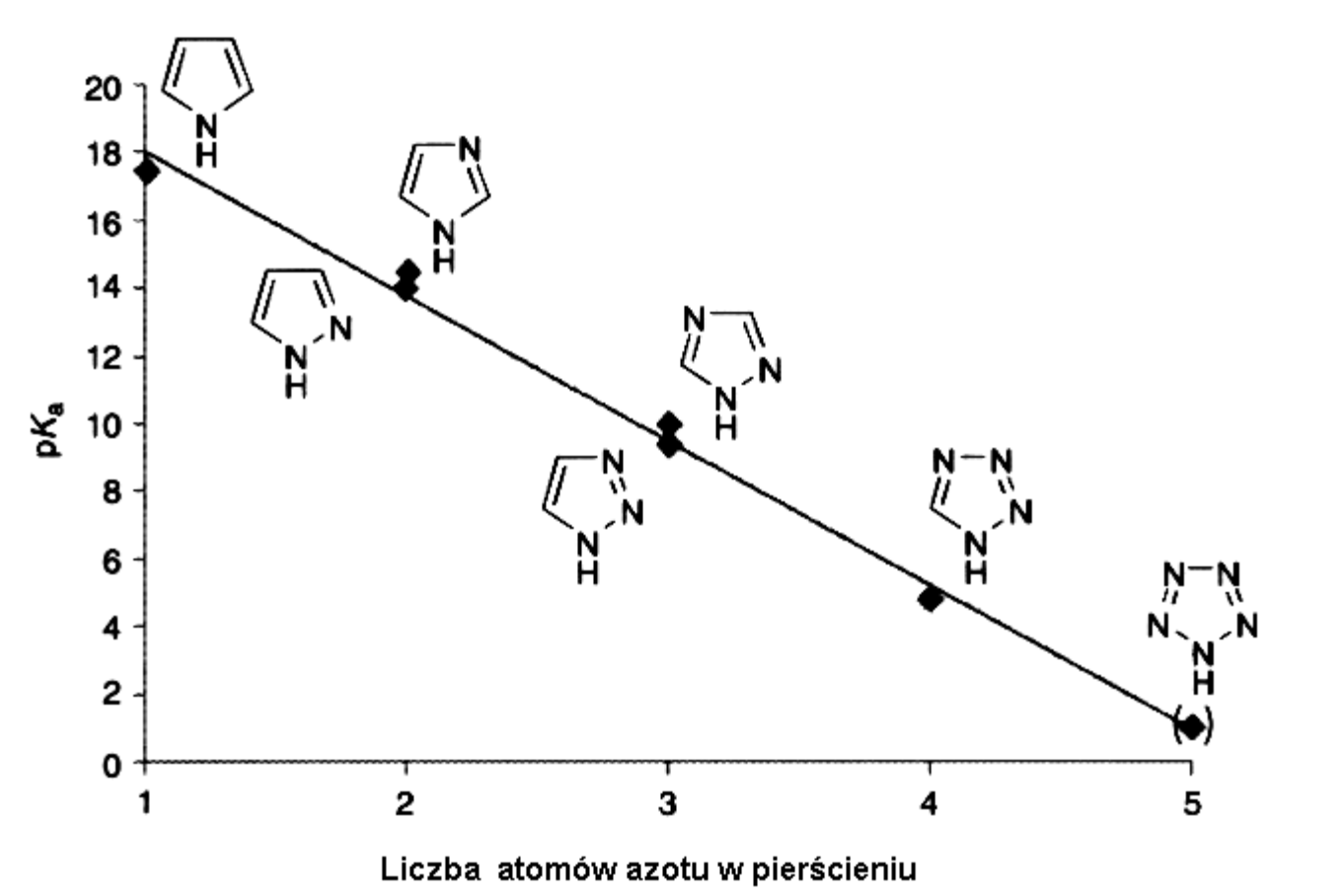
1*H*-1,2,4-triazol



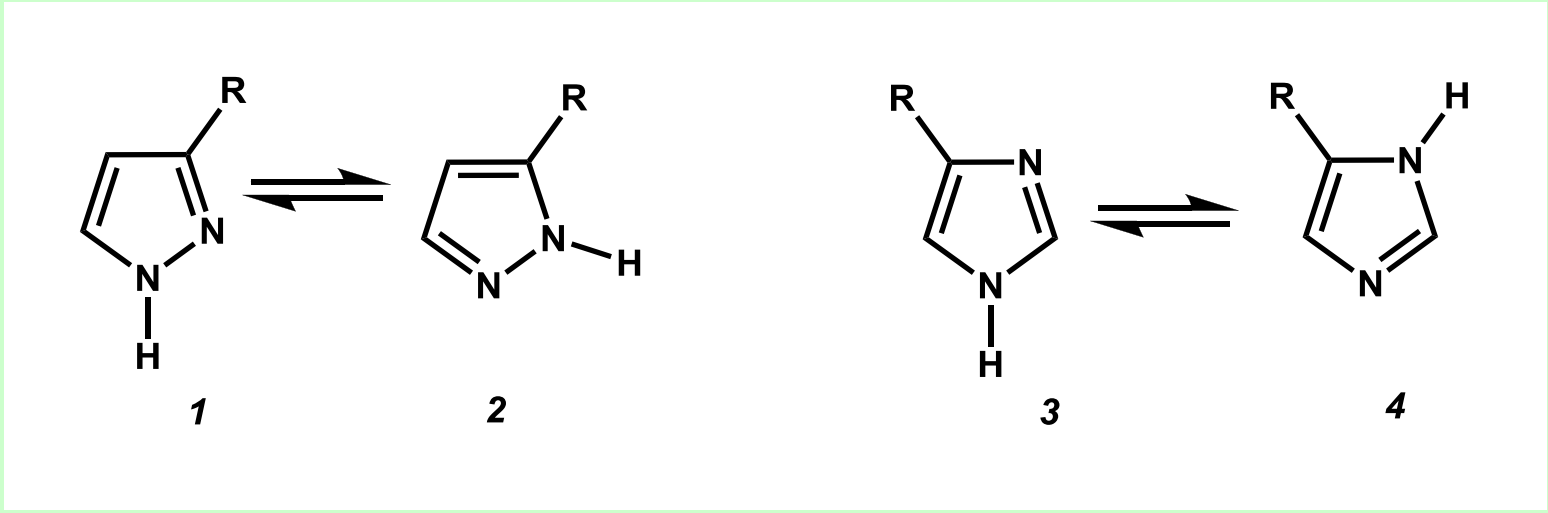
1*H*-tetrazol

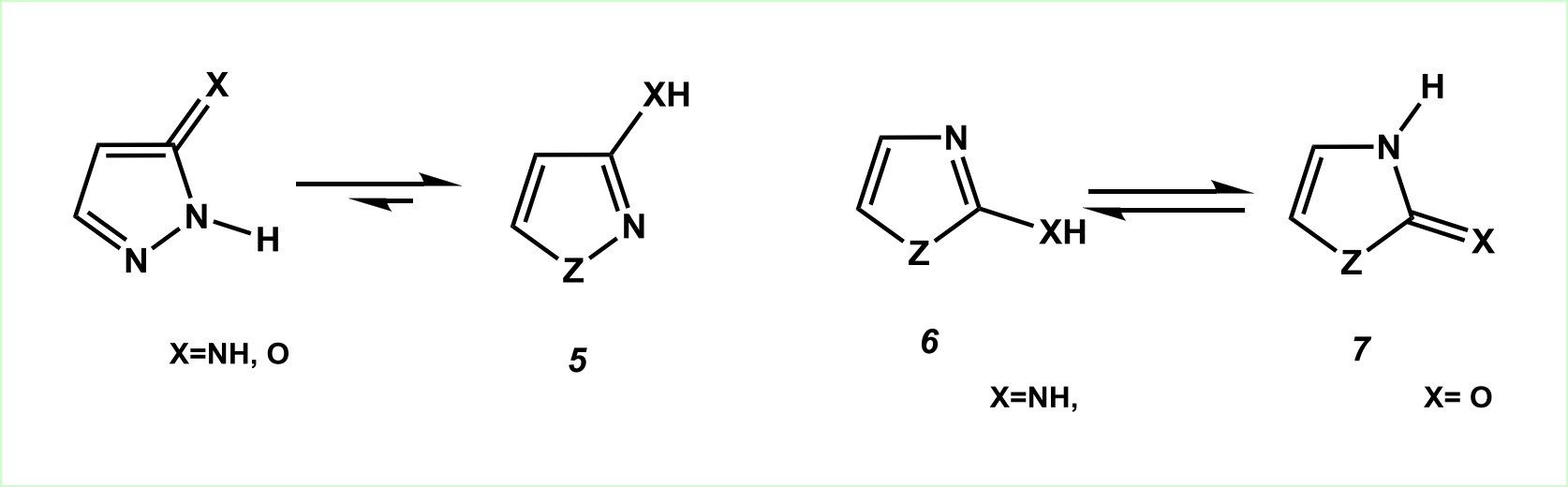


2*H*-tetrazol

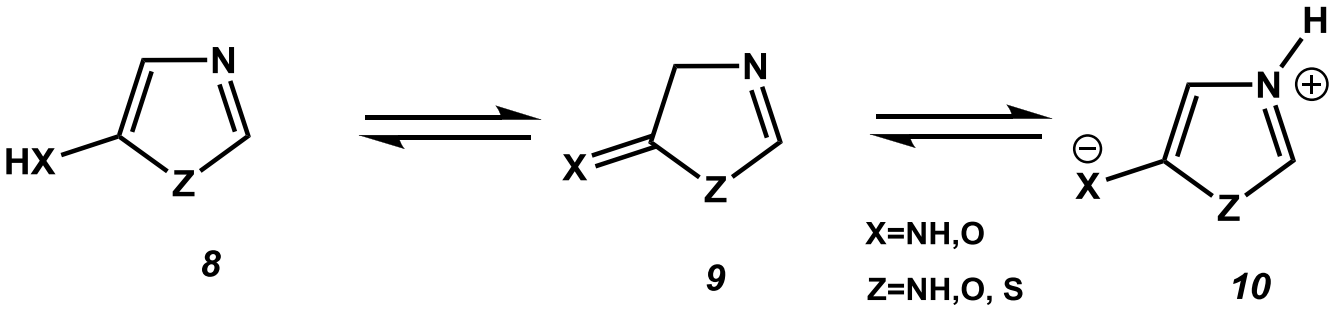

20
18
16
14
12
10
8
6
4
2
0
pKa
1
2
3
4
5
Liczba atomów azotu w pierścieniu

Tautomeria annularna w azolach



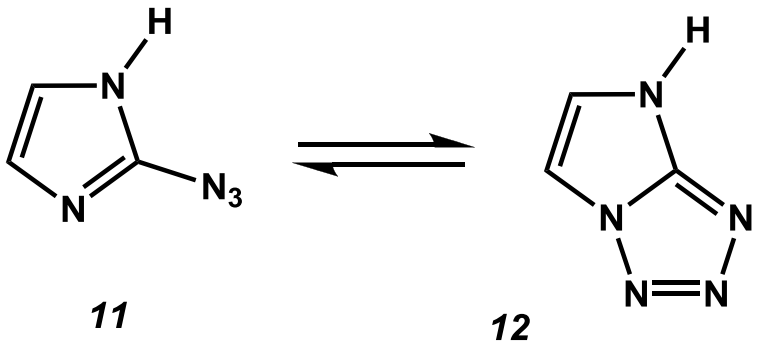


Azole podstawione w pozycjach 4,5

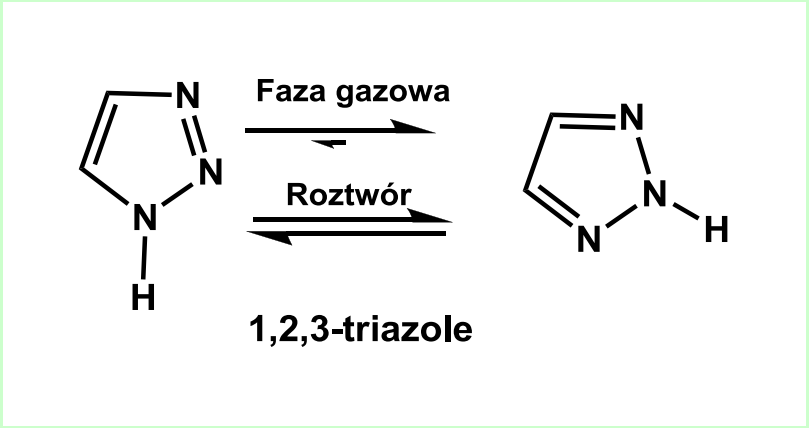


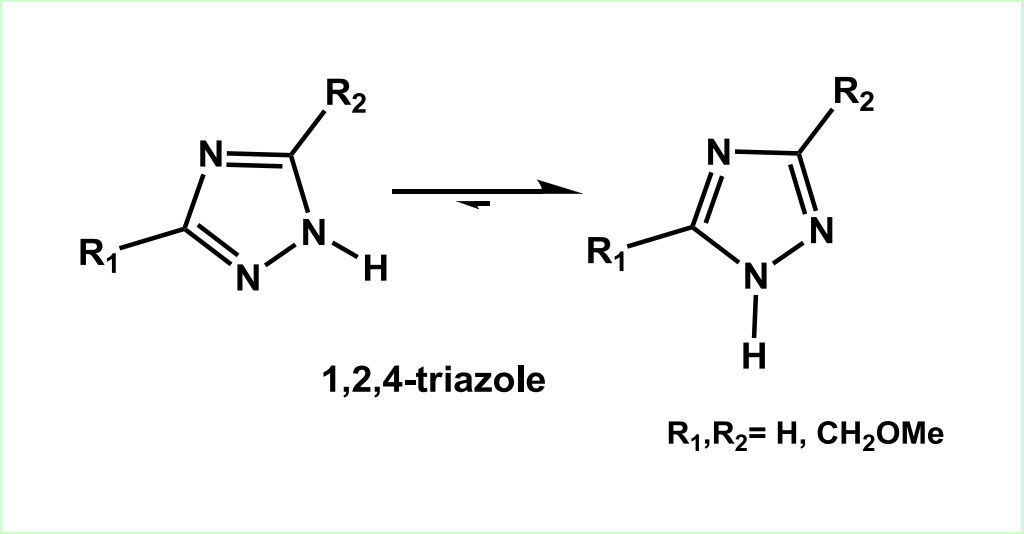
8 *9* *10*

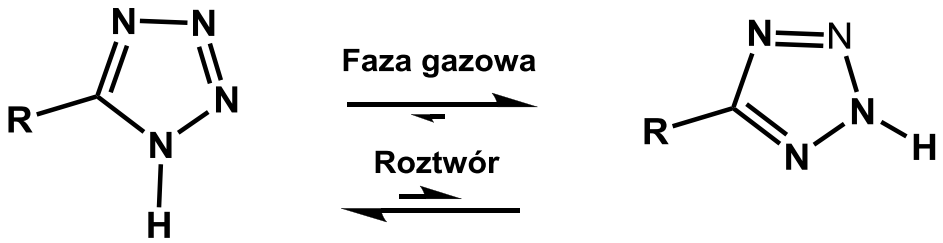
Tautomeria pierścieniowo-łańcuchowa



11 *12*


Faza gazowa
Roztwór
1,2,3-triazole


1,2,4-triazole
R1,R2= H, CH2OMe

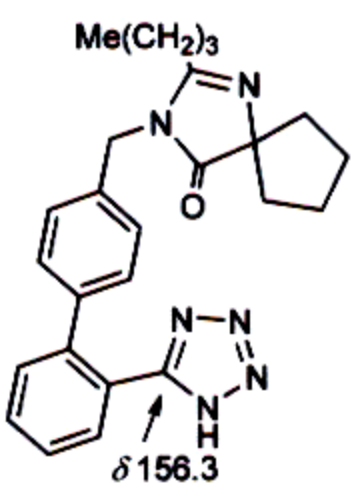


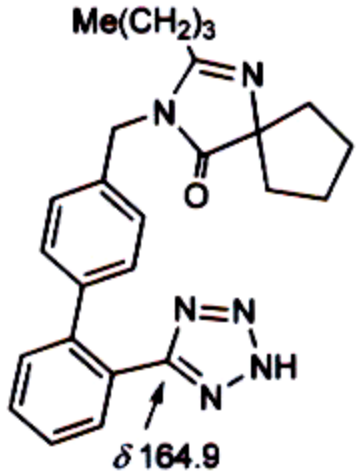
1*H*-tetrazole

2*H*-tetrazole

R= H, CH_3, CD_3, CF, NH_2

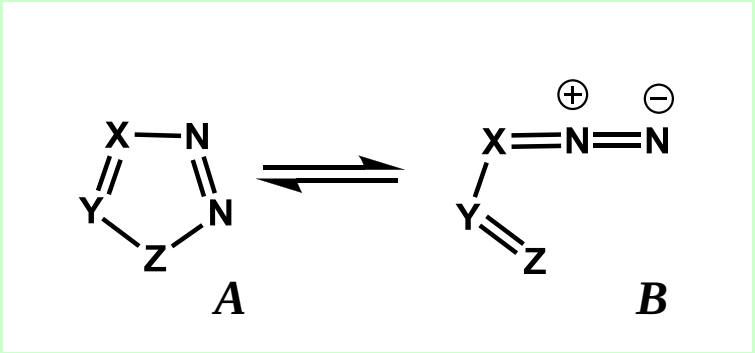
irbesartan forma A

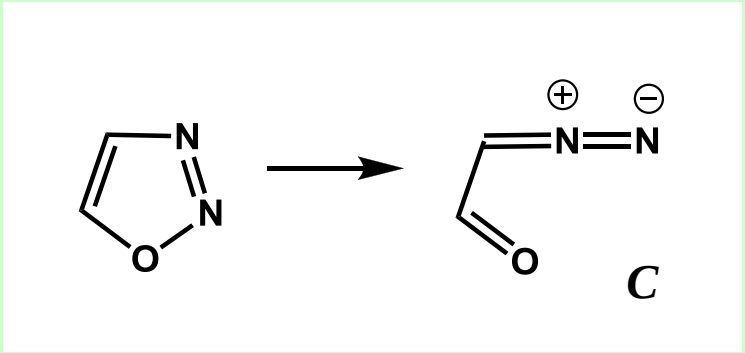


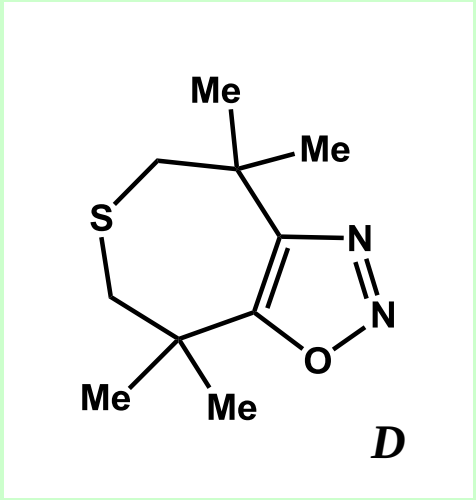


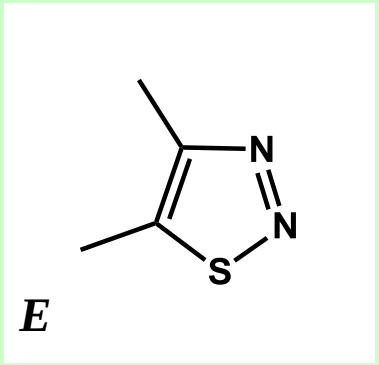
irbesartan forma B

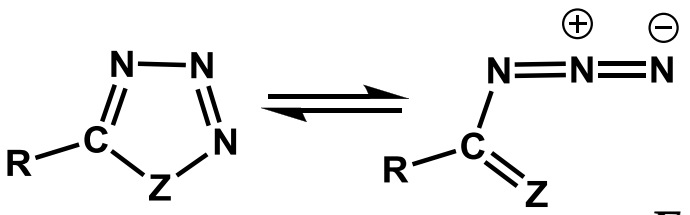
Tautomeria walencyjna w azolach





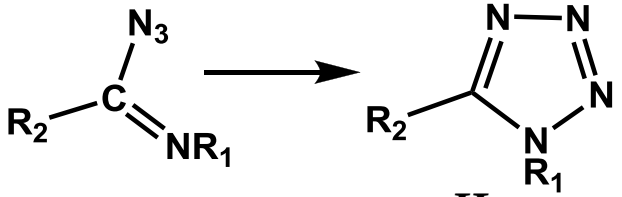






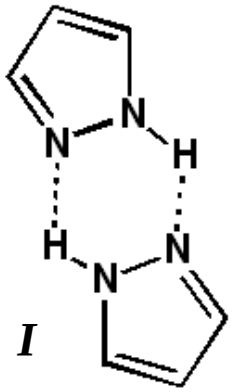
F

Z= O, S, NR

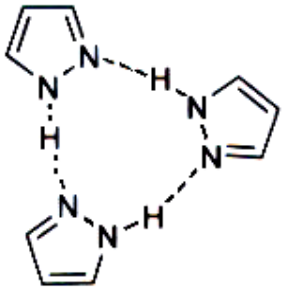


G *H*

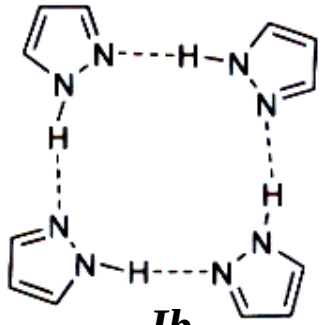
Asocjaty



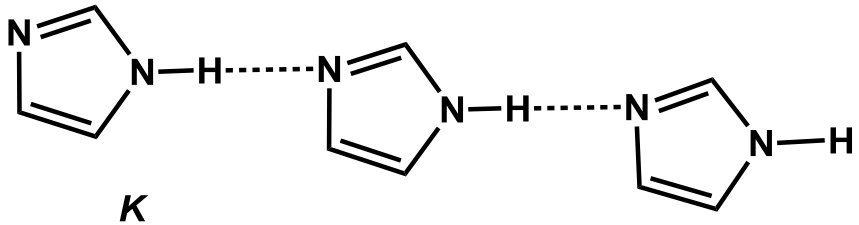
I



Ia



Ib

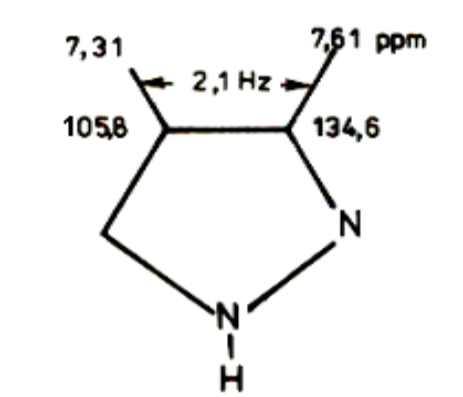


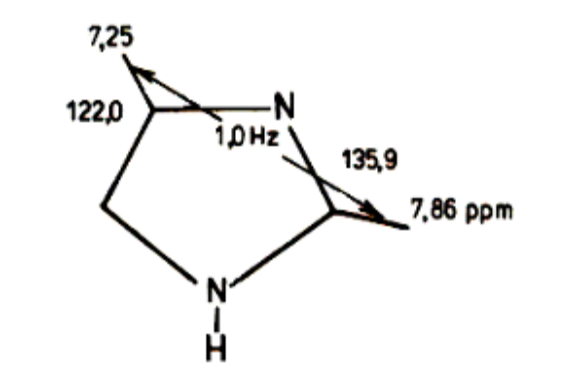
K

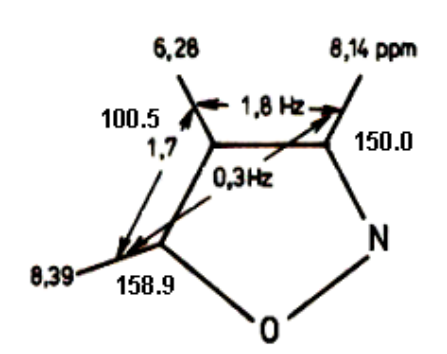
Widma NMR – charakterystyczne cechy ułatwiające określanie struktury

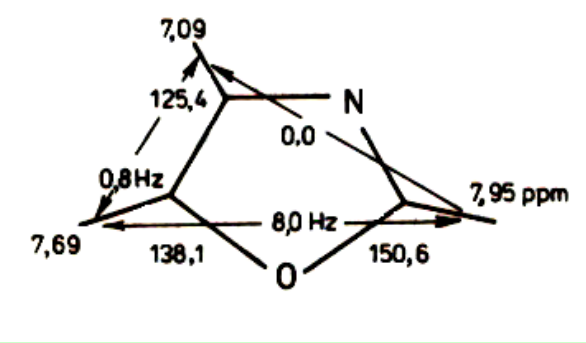
AZOLI

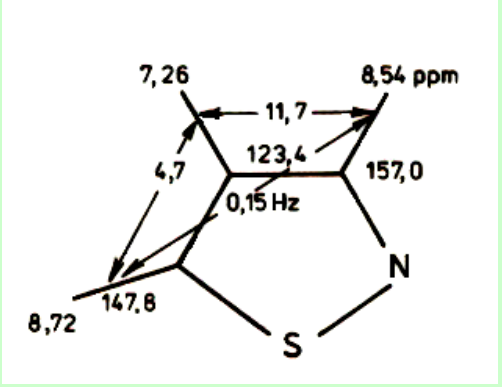
^{1}H NMR i ^{13}C NMR

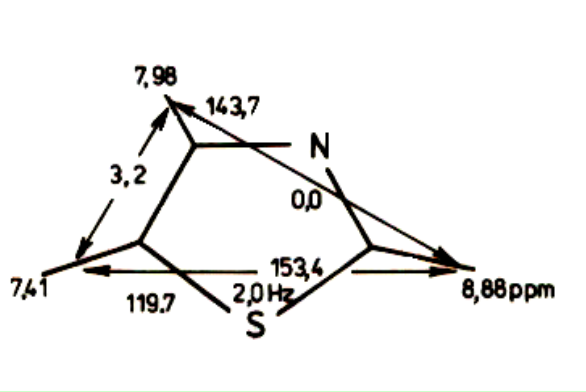




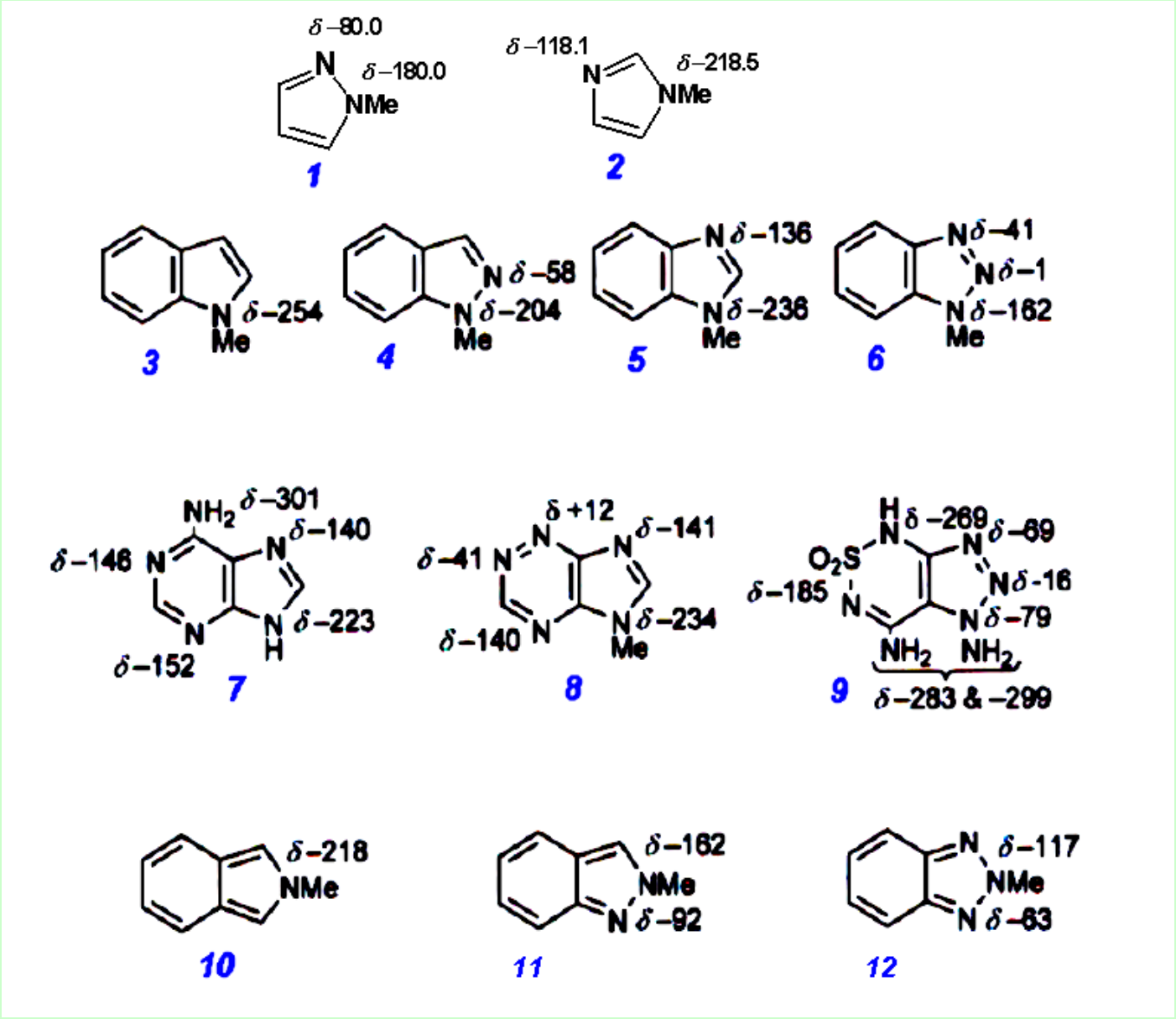




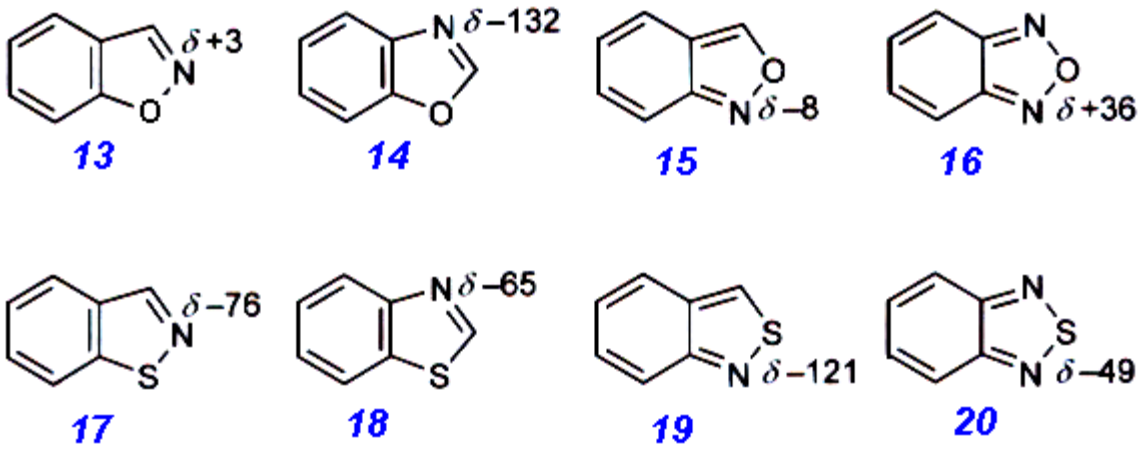




^{15}N NMR


δ –80.0
N
δ –180.0
NMe
1
δ –118.1
N
δ –218.5
NMe
2
N
δ –254
Me
3
N δ –58
N δ –204
Me
4
N δ –136
N δ –236
Me
5
N δ –41
N δ –1
N δ –162
Me
6
NH2 δ –301
δ –140
δ –146 N
N
N
H δ –223
δ –152
7
δ +12
δ –141
δ –41 N
N
N
δ –140 N
N δ –234
Me
8
H δ –269
N
δ –69
O2S
N
δ –185
N δ -16
N δ –79
NH2 NH2
δ –283 & –299
9
δ –218
NMe
10
δ –162
NMe
N δ –92
11
N δ –117
NMe
N δ –63
12

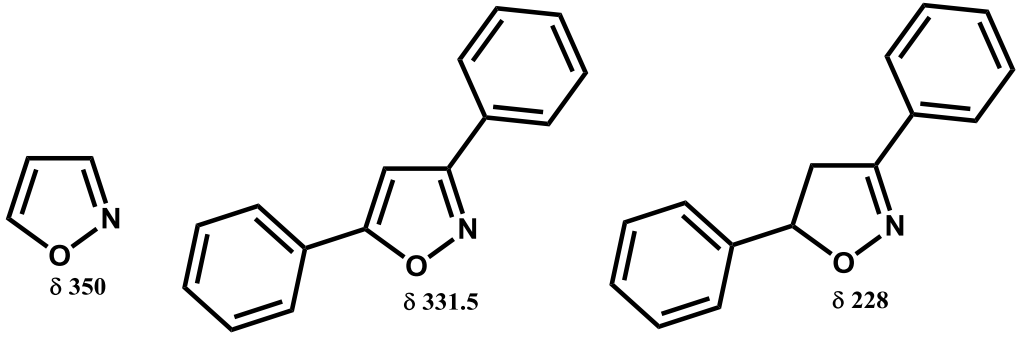
^{15}N NMR

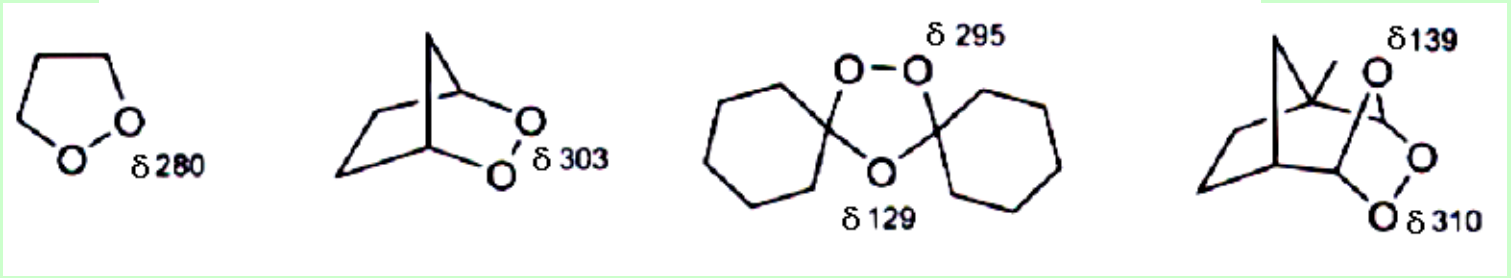


13 14 15 16

17 18 19 20

^{17}O NMR





Widma IR – charakterystyczne cechy ułatwiające określanie struktury

AZOLI

Azole częstotliwość drgań w zakresie 1650- 1300 cm^{-1}

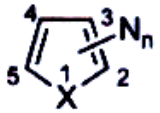
związek	częstotliwość (cm^{-1})			
Isoxazoles	1650–1610	1580–1520	1510–1470	1460–1430
Isothiazoles	–	–	1488	1392
Pyrazoles	–	1600–1570	1540–1510	1490–1470
Oxazoles	1650–1610	1580–1550	1510–1470	1485
Thiazoles	1625–1550	–	1550–1470	1440–1380
Imidazoles	1605	1550–1520	1500–1480	1470–1450
1,2,4-Oxadiazoles	–	1590–1560	–	1470–1430
1,2,5-Oxadiazoles	–	1630–1560	1530–1515	1475–1410
1,3,4-Oxadiazoles	1680–1650	1630–1610	1600–1580	1430–1410
1,2,4-Thiadiazoles	–	1590–1560	1540–1490	–
1,2,3-Thiadiazoles	1650–1590	–	1560–1420	1350–1325
1,2,5-Thiadiazoles	–	–	–	1461
1,2,3,4-Thiatriazoles	1720–1690	1610–1530	–	–
1,2,3-Triazoles	1650–1615w	–	1530–1485	1440w
1,2,4-Triazoles	–	–	1545–1535	1470–1460
Tetrazoles	1640–1615	–	1450–1410	1400–1335

Widma UV – charakterystyczne cechy ułatwiające określanie struktury

AZOLI

Widma azoli w nadfiolecie podobne są do widm pięcioczłonowych związków heteroaromatycznych z jednym heteroatomem. Zastąpienie fragmentu CH przez atom N ma mały wpływ na charakter widma. Azaanalogi pirolu wykazują λ_{max} 217 nm lub niżej (log ε ≈ 3,5), azaanalogi tiofenu λ_{max} 230-260 nm (log ε ≈ 3,7 a azaanalogi furanu λ_{max} poniżej 220 nm (log ε ≈ 3,5) .

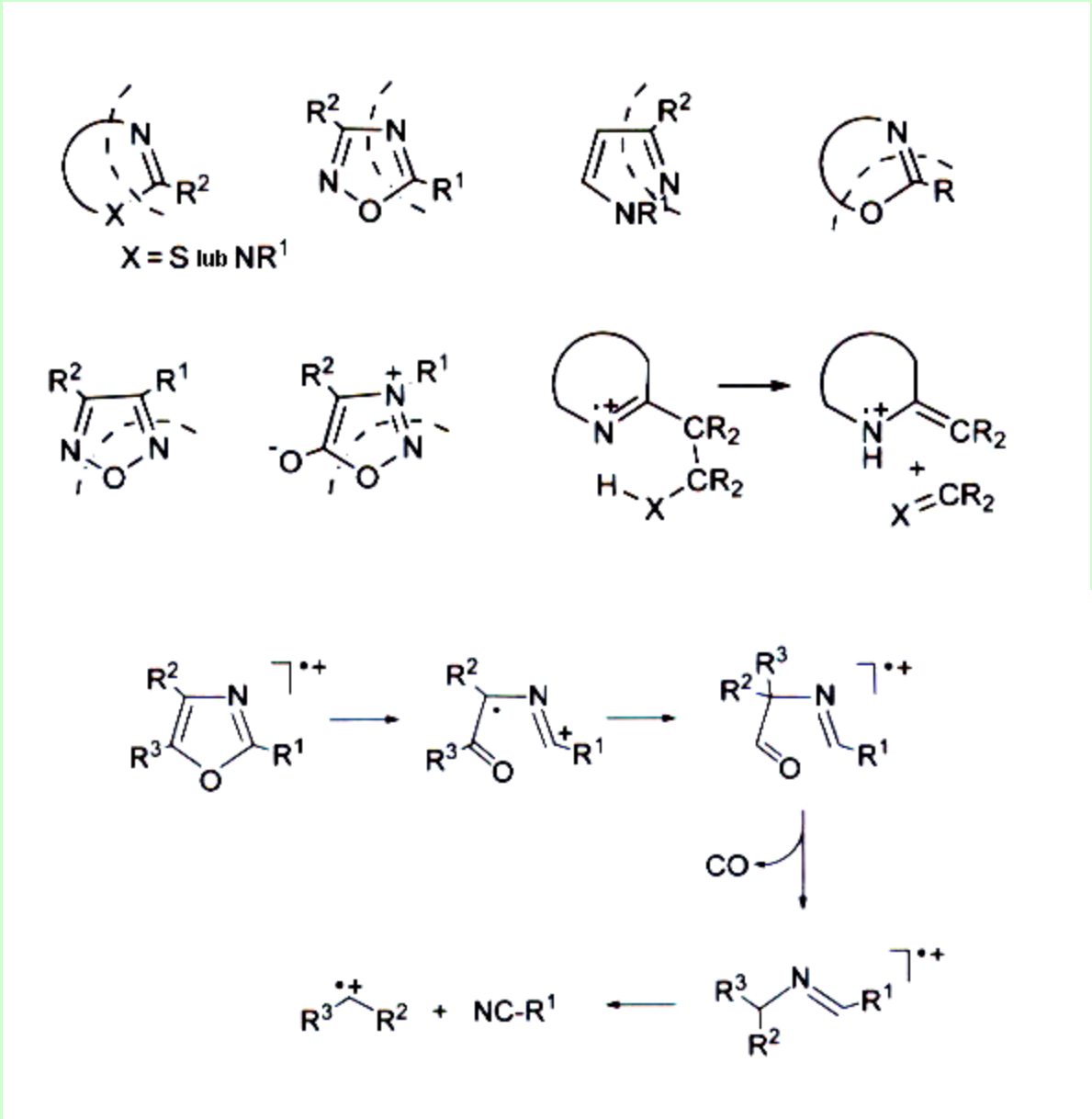
Widma UV –pasma absorpcji dla azoli



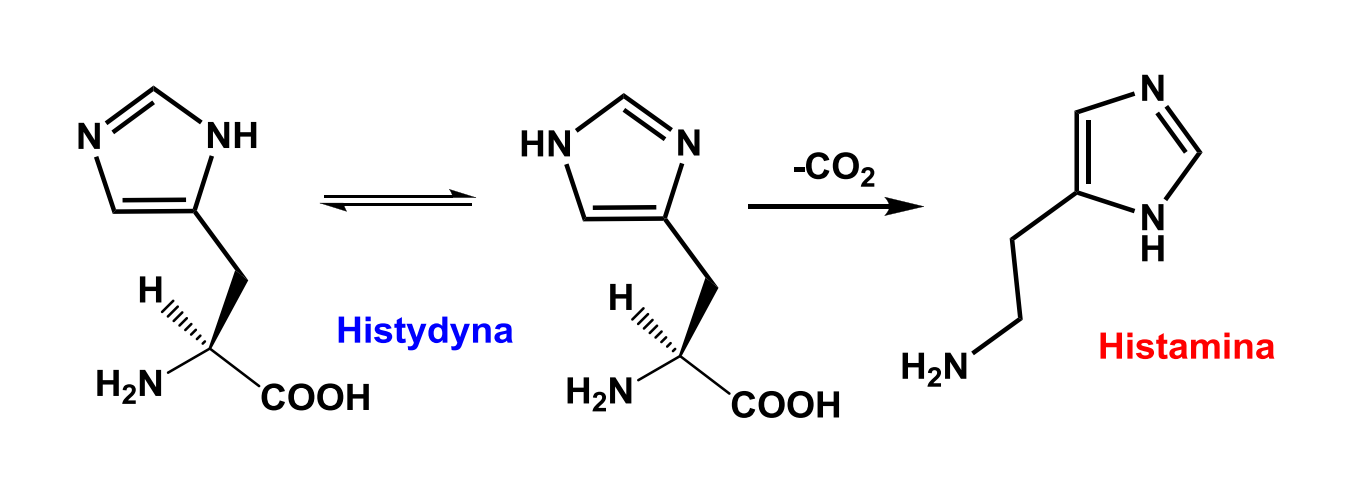
	X = NH	*X = O*	*X = S*
Pochodne	*λ_{max}(nm) (log ε)*	*λ_{max}(nm) (log ε)*	*λ_{max}(nm) (log ε)*
No N	210 (4.20)	208 (3.90)	215 (3.80), 231 (3.87)
2-Aza	210 (3.53)	211 (3.60)	244 (3.72)
3-Aza	207–208 (3.07) End absorption	240	207.5 (3.41), 233 (3.57)
2,3-Diaza	210 (3.64)	–	211 (3.64), 249 (3.16), 294 (2.29)
2,4-Diaza	216.5 (3.66)	–	229 (3.73)
2,5-Diaza	–	220	250 (3.86), 253 (3.87), 257 (2.83), 260 (3.68)
3,4-Diaza	–	200	220
2,3,4-Triaza	205	–	280 (4.03)

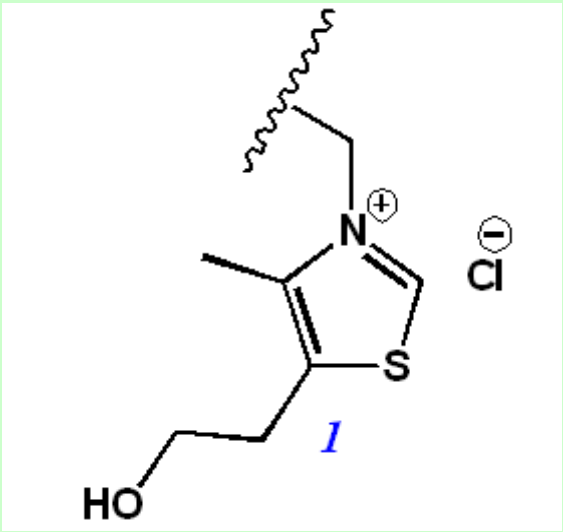
Widma mas – charakterystyczne cechy ułatwiające określanie struktury

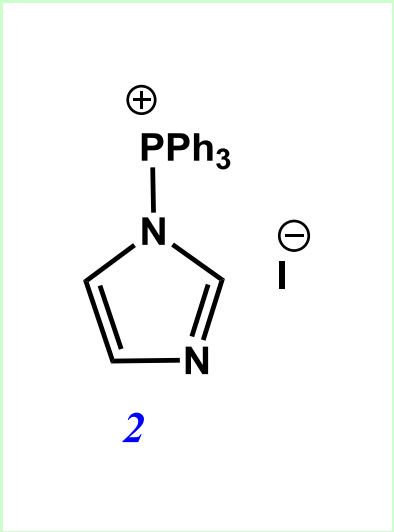
AZOLI

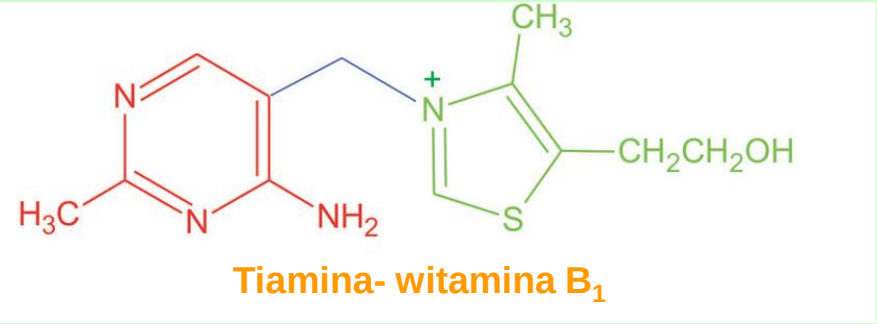


Zastosowanie i znaczenie biologiczne AZOLI

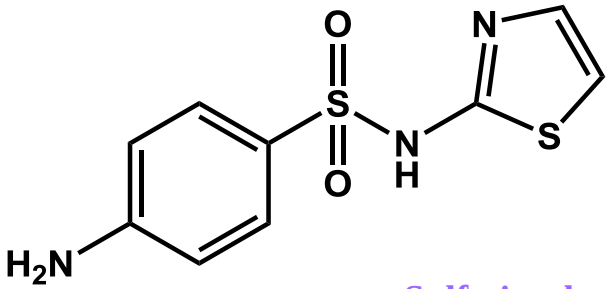




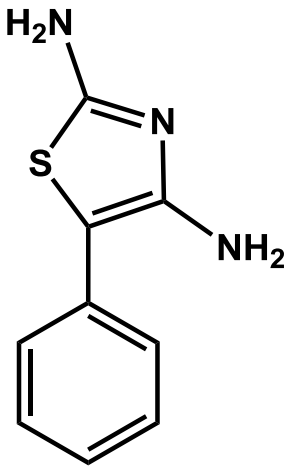




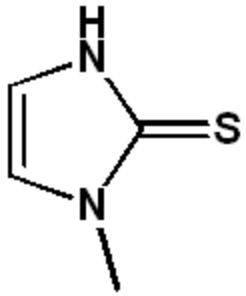
Kazimierz Funk– polski biochemik, twórca nauki o witaminach. Odkrył i wyodrębnił z otrąb ryżowych pierwszą witaminę B_1 w początkch XX wieku . Funk jest autorem terminu "witamina" (łac. *vita – życie, tiamina – substancja).*



Sulfatiazol

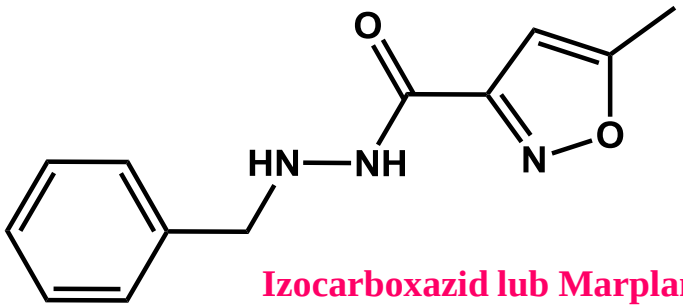


Amiphenazol



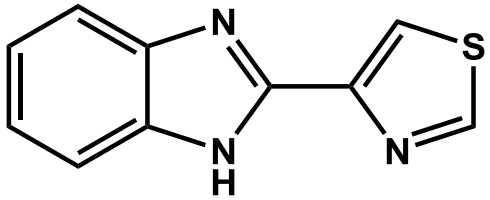
Thiamazol, Metizol

(tyrostatyk)



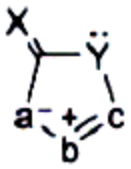
Izocarboxazid lub Marplan

(tymoleptyk)

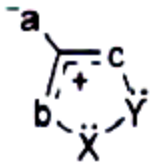


Thiabendazol

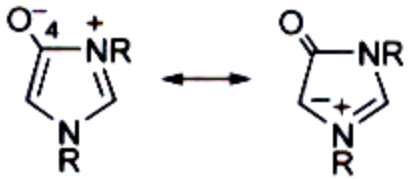
ZWIĄZKI MEZOJONOWE



Typ A

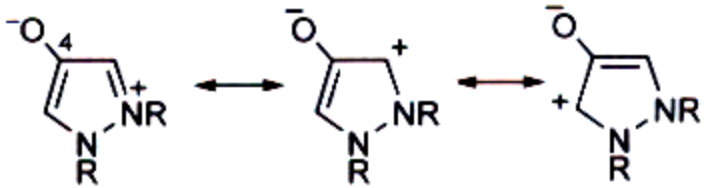


Typ B



imidazolilio-4-olan

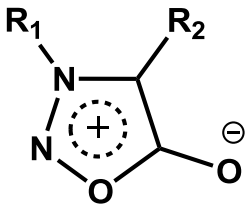
Typ A



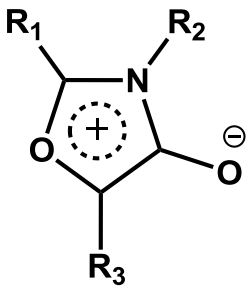
pirazolilio-4-olan

Typ B

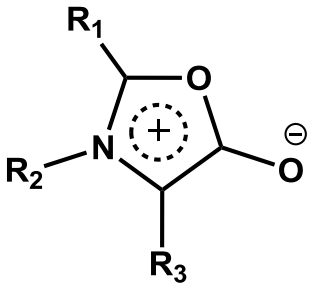
Do typu A należą pochodne sydnonów (1), oksazoli (2,3), oksatioli (4,5), imidazoli (6) i innych 1,3-azoli. Przedstawicielami związków mezojonowych grupy B są pochodne pirazoli, ditioli (7), tetrazoli (8).



1



2



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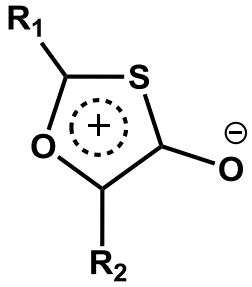
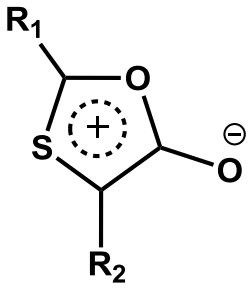
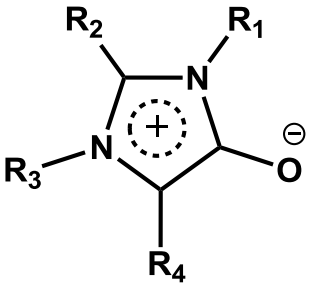


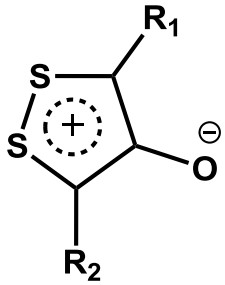
4



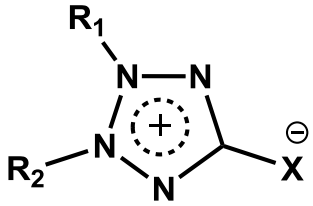
5



6

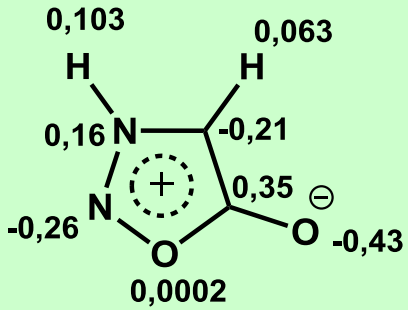


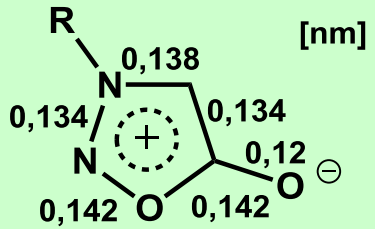
7



8

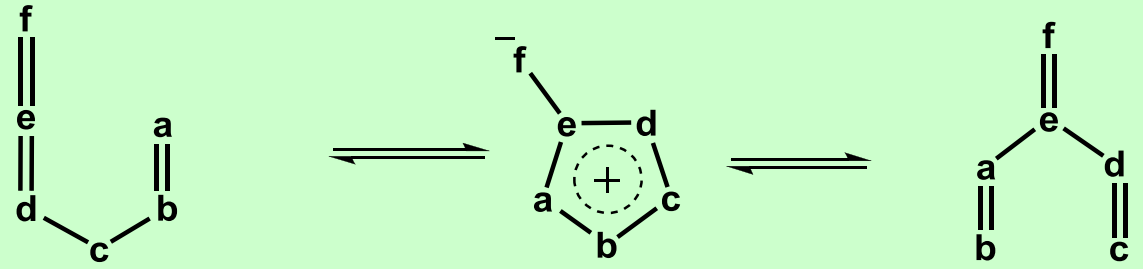
X=-O,-S,-N-NO


0,103
0,063
H
H
0,16
N
-0,21
0,35
N
-0,26
O
-0,43
O
0,0002


R
[nm]
0,138
N
0,134
0,134
0,12
N
O
0,142
0,142
O

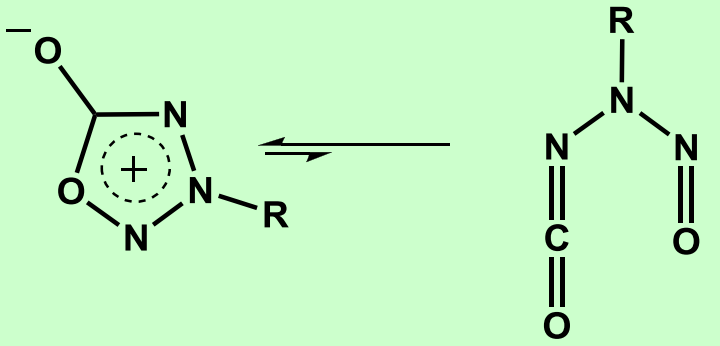
•**Związki mezojonowe mogą istnieć w równowadze tautomerycznej z ich izoelektronowymi łańcuchowymi analogami, przy czym w przypadku związków z grupy A przeważa na ogół forma cykliczna.**

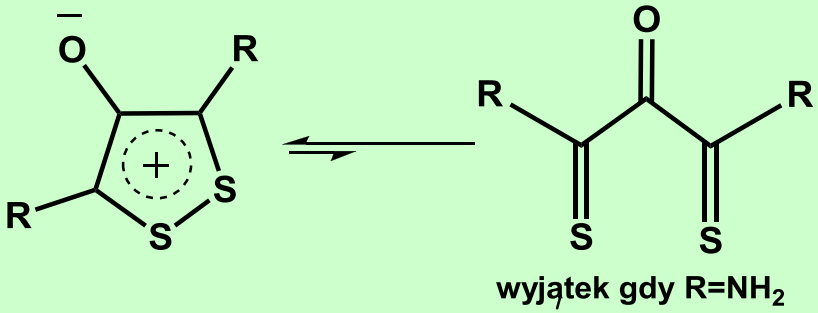
•**Dla typu B formą podstawową może być zarówno forma cykliczna-tetrazol- jak i łańcuchowa, co obserwuje się w przypadku triketonu.**



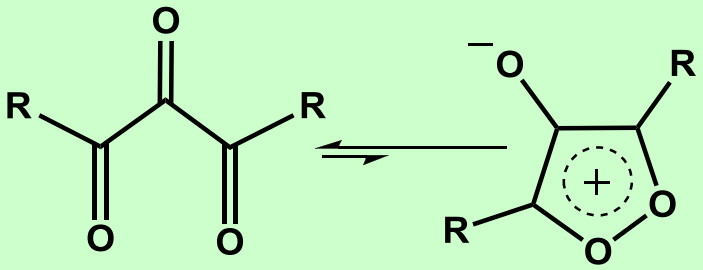
Typ A

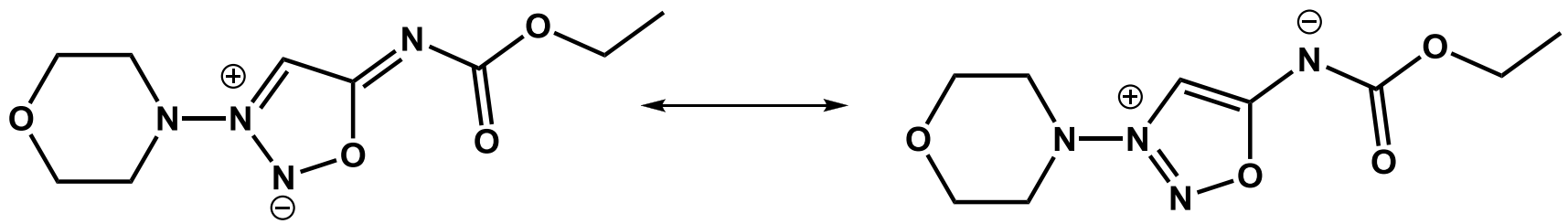
Typ B



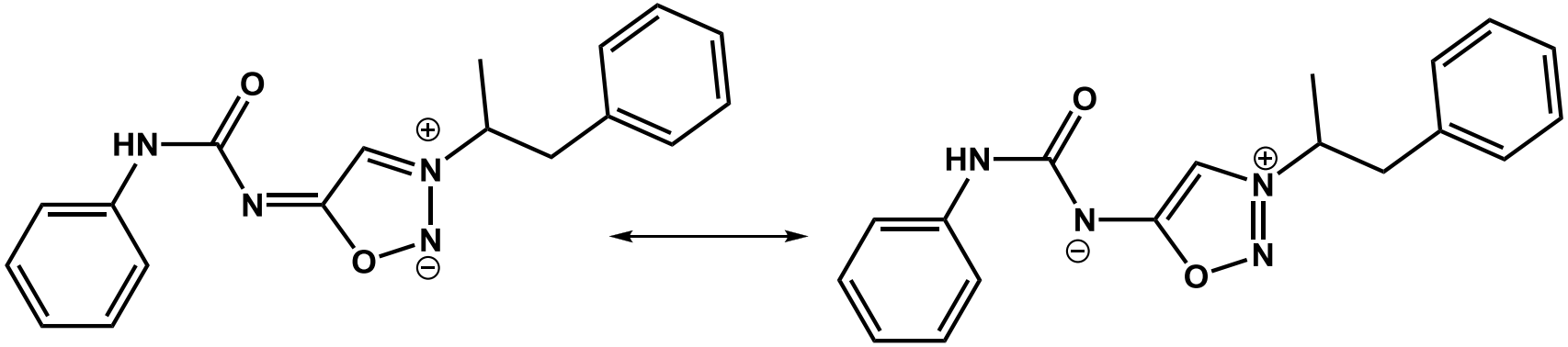


wyjątek gdy R=NH_2





Molsidomin



Sydnokarb