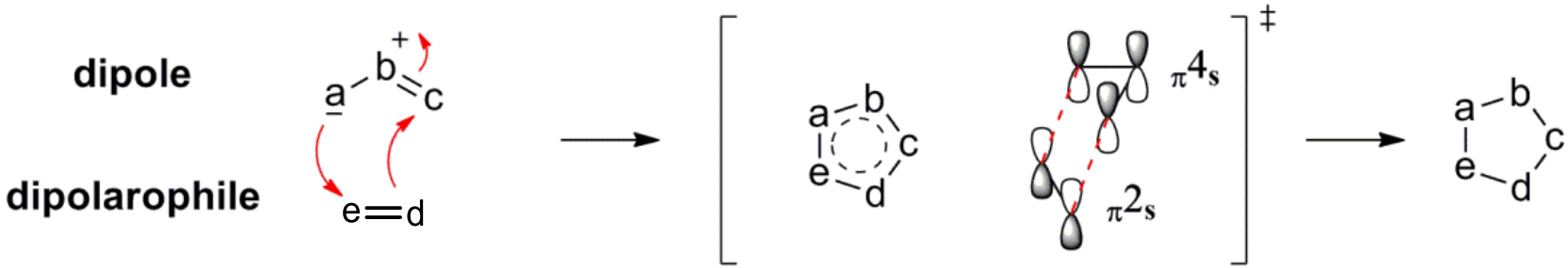
Азиридины в реакциях 1,3-диполярного циклоприсоединения

М.А. Кузнецов, А.С. Панькова
СПбГУ, Институт химии

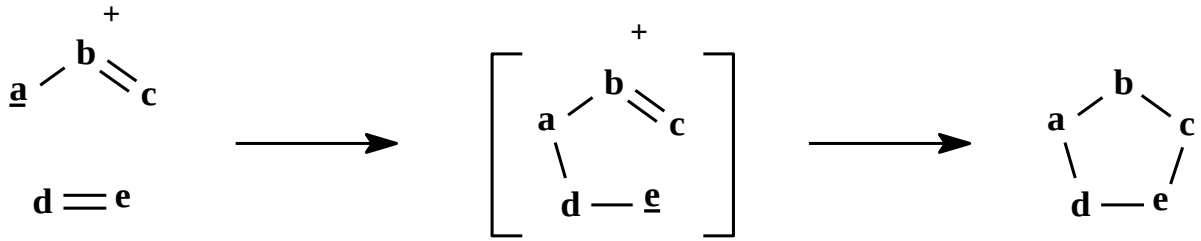
Санкт-Петербург

1,3-Диполярное циклоприсоединение



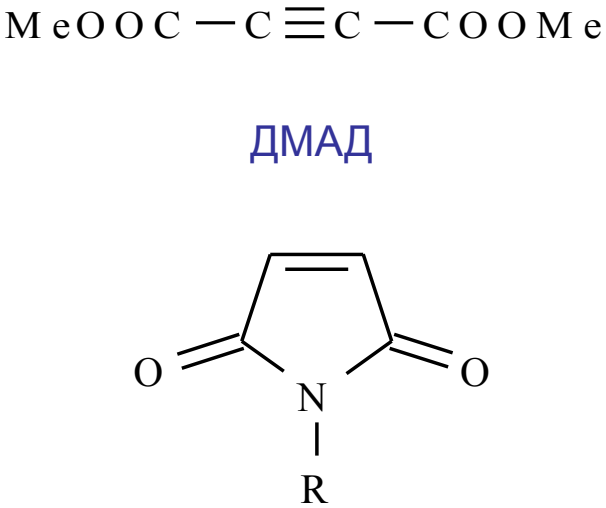
Rolf Huisgen. 1,3-Dipolar Cycloadditions. Past and Future.
Angew. Chem. Int. Ed. **2**(10), 565–598 (1963)

Механизмы: согласованный (выше) и постадийный (ниже)

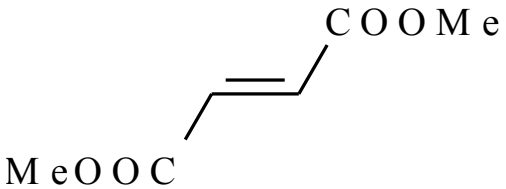


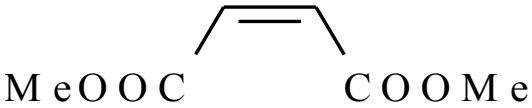
Диполярофилы

В принципе, соединения с почти любыми двойными или тройными связями X=Y или C≡Y: C=C, C≡C, C=N, C≡N, N=N, C=O, C=S с электроноакцепторными (реже – с донорными) заместителями.
Стандартные: ДМАД, диметилмалеат, диметилфумарат, малеимиды.

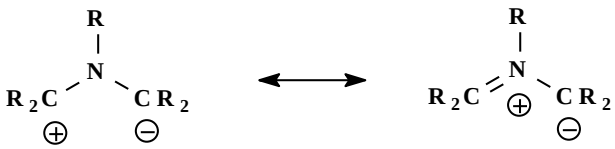


ДМАД

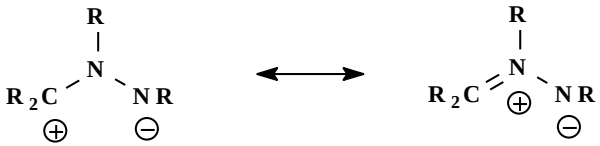




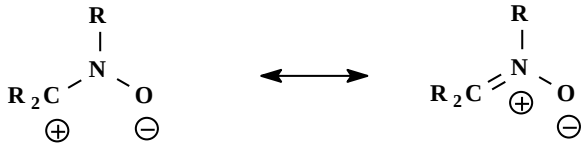
Диполи



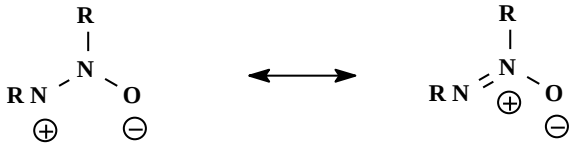
Азометинилиды



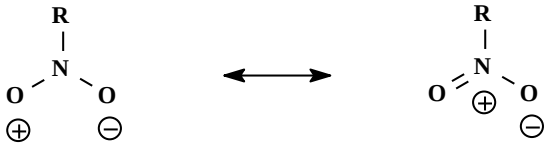
Азометинимины



Нитроны-



Азоксисоединения



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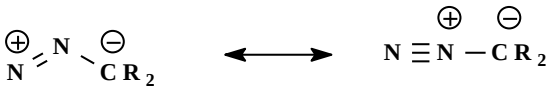
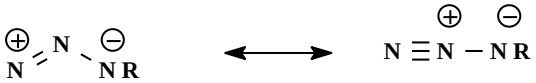
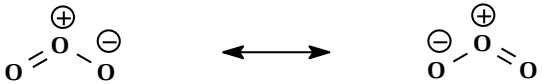


Диазоалканы

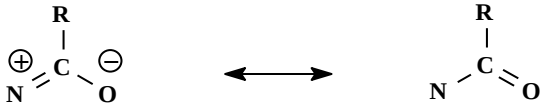


Азиды



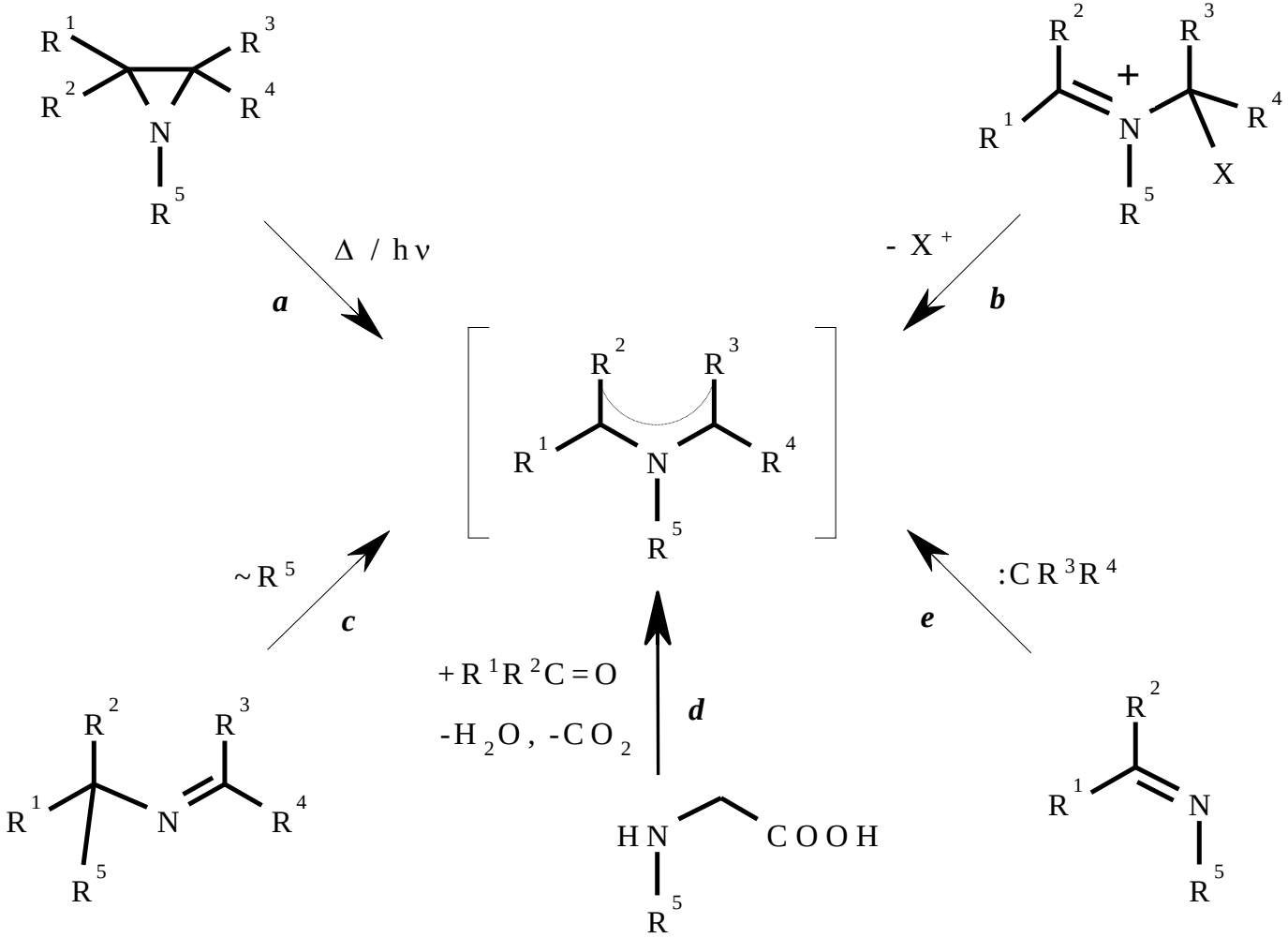
Озон-

1,3-диполи без октетной стабилизации

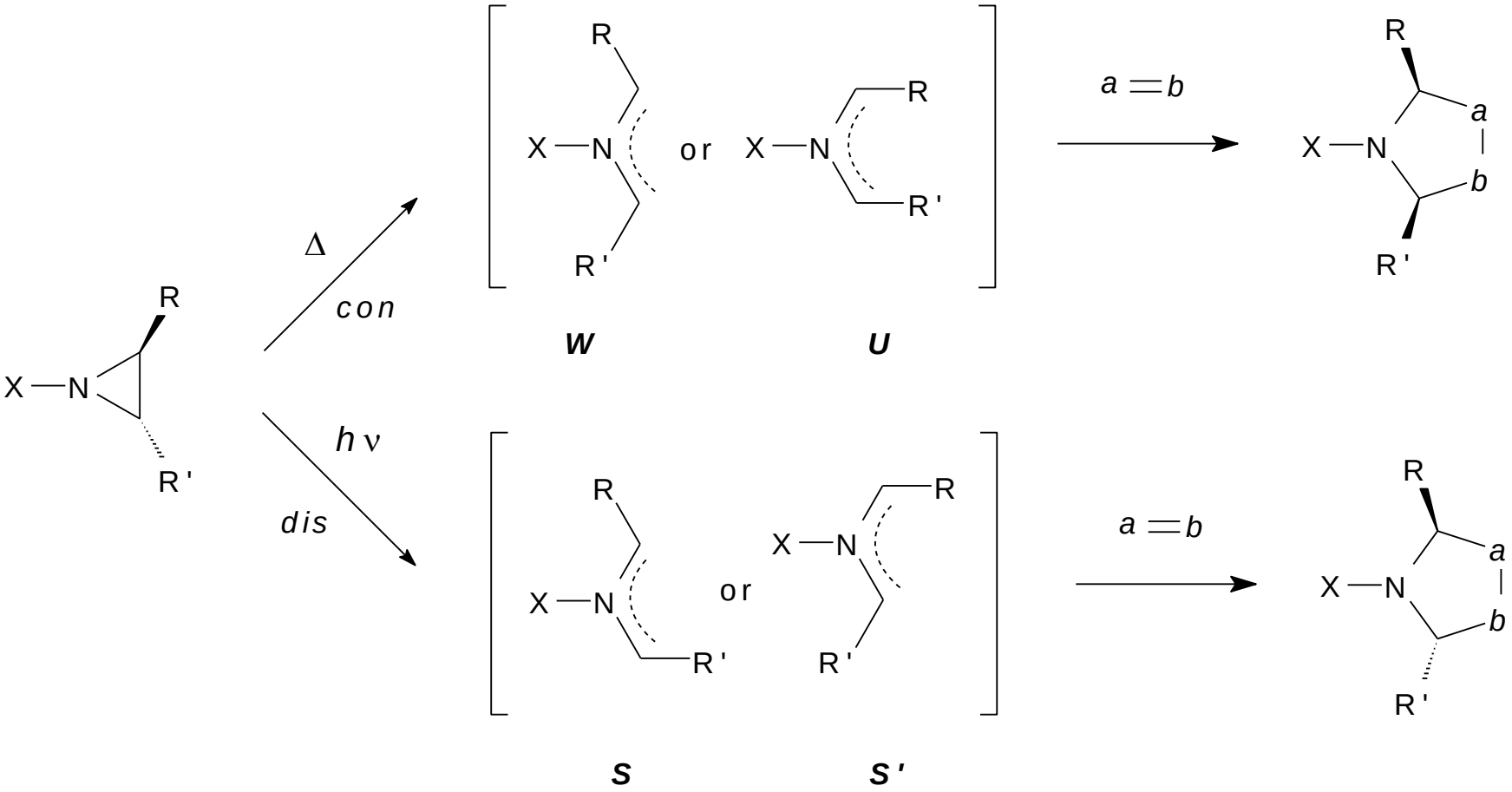


Кетонитрены

Методы генерирования азометинилидов

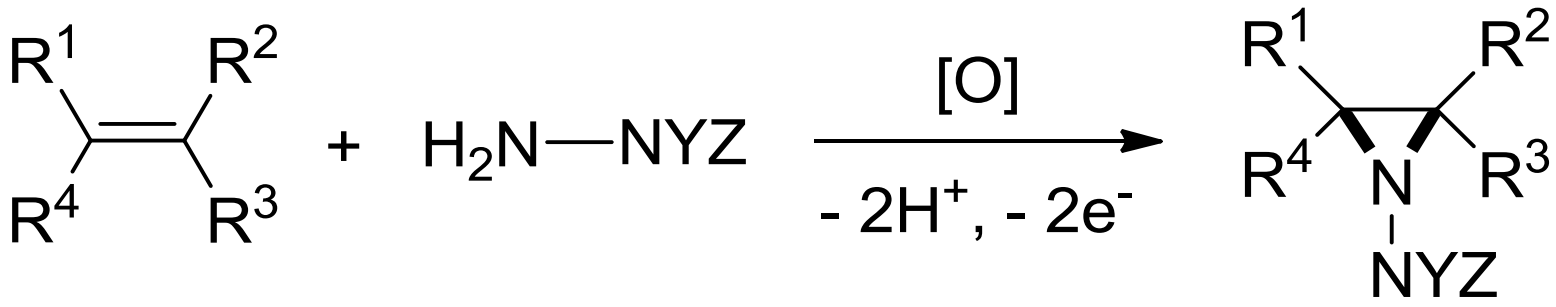


Азиридины в реакциях 1,3-диполярного циклоприсоединения

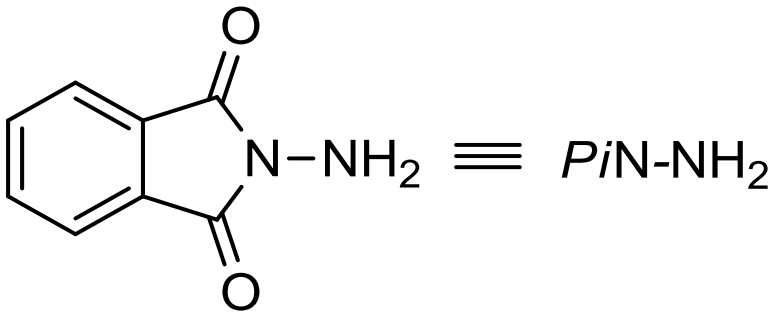


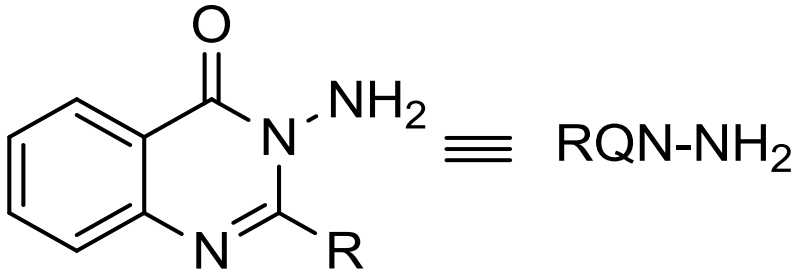
H.W. Heine, R. Peavy, 1965
R. Huisgen *et.al.*, 1967

Окислительное аминоазиридинирование

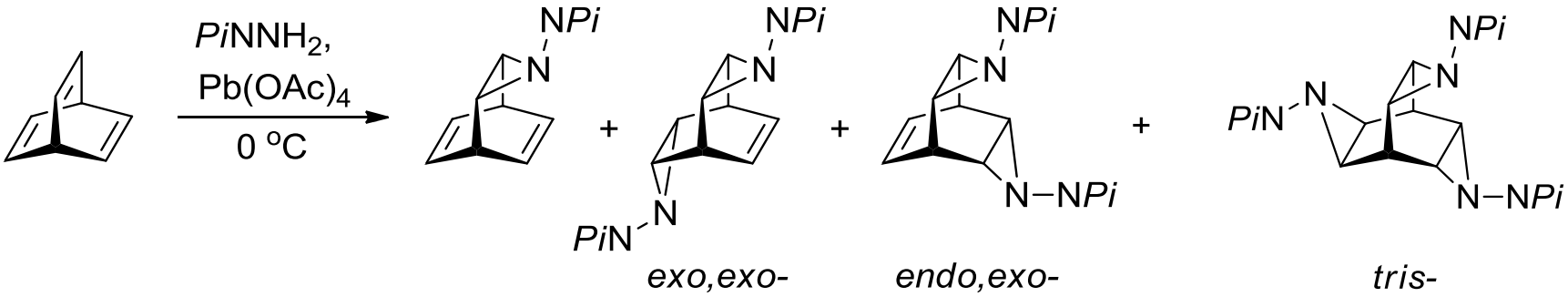


N-Аминосоединения

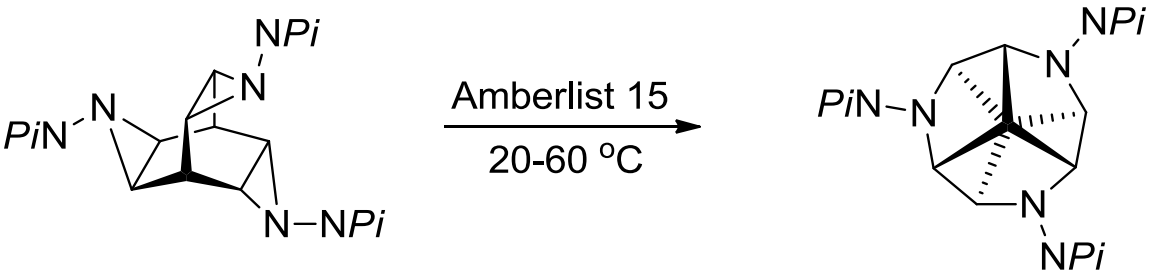




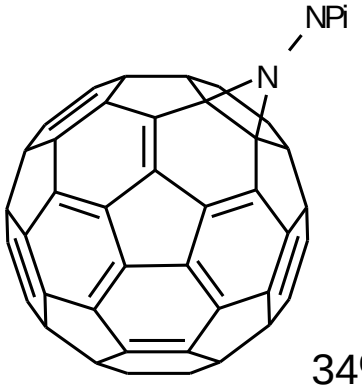
Реакции с барреленом и фуллереном



19% with 24-fold excess of reagents



75%

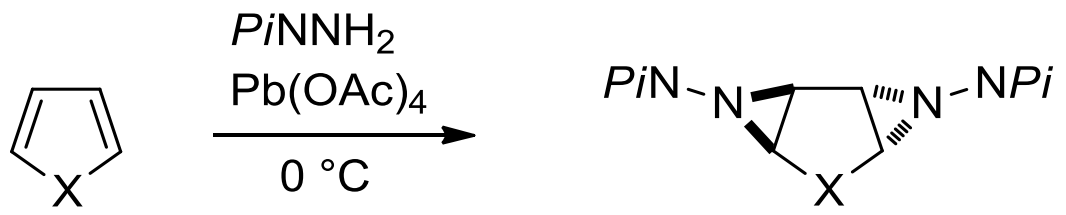


34%

Eur. J. Org. Chem. **2006**, 2590–2600

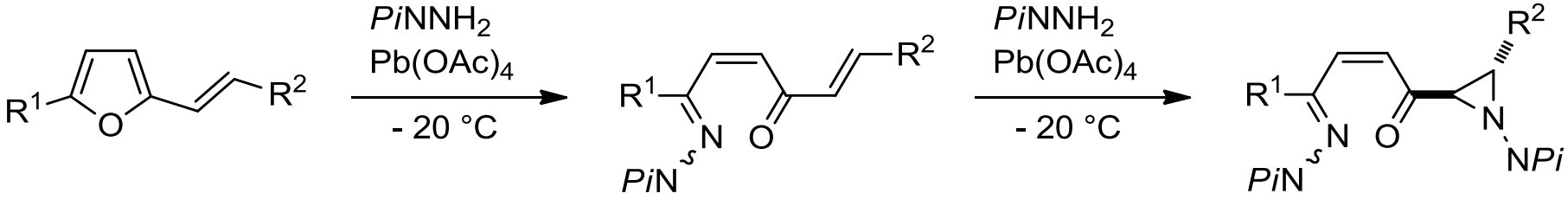
Tetrahedron Lett. **1994**, *35*, 4371-4374

Присоединение к гетероциклам



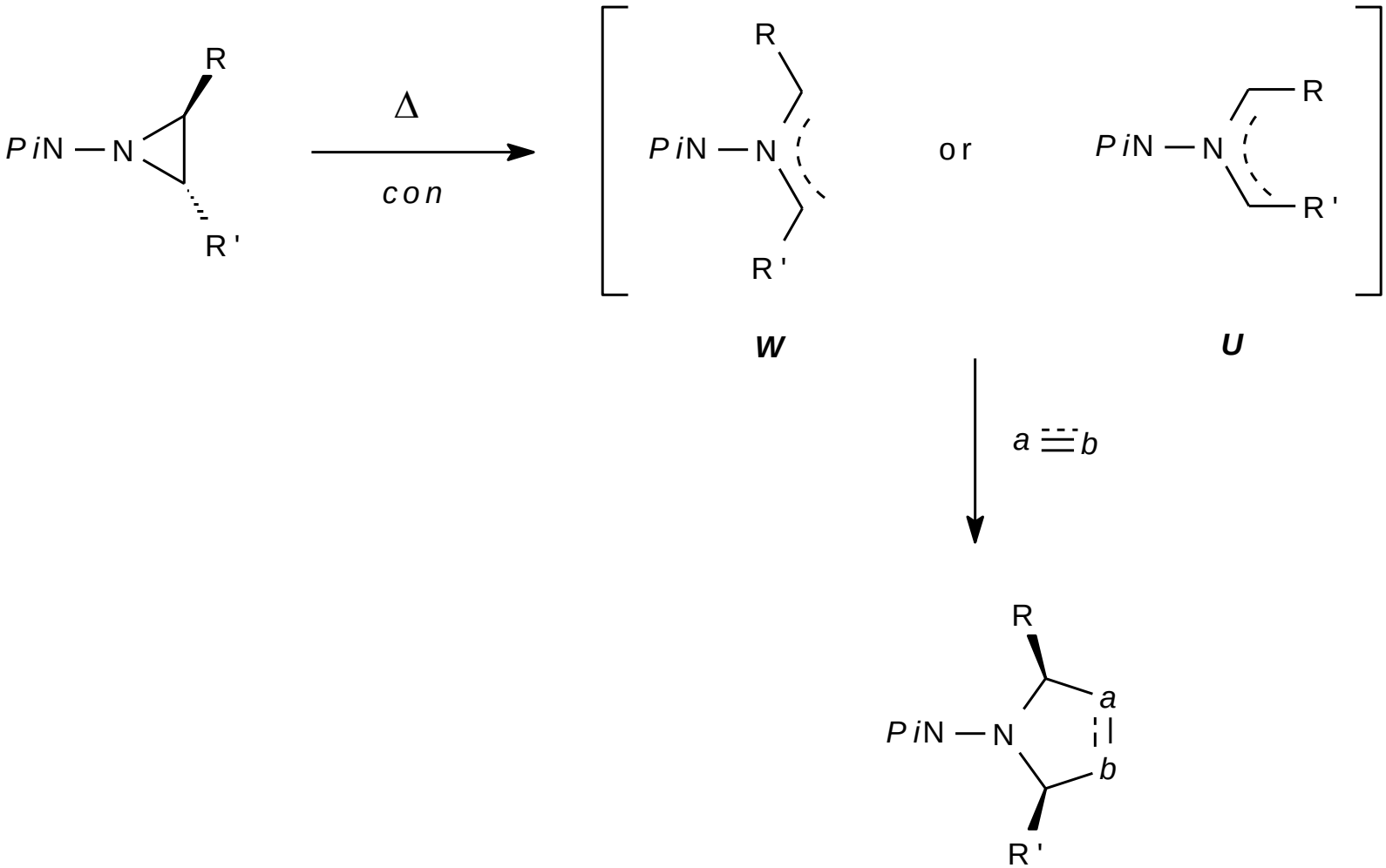
X = S (15%), Se (18%)

Tetrahedron Lett. **2011**, *52*, 4048-4050

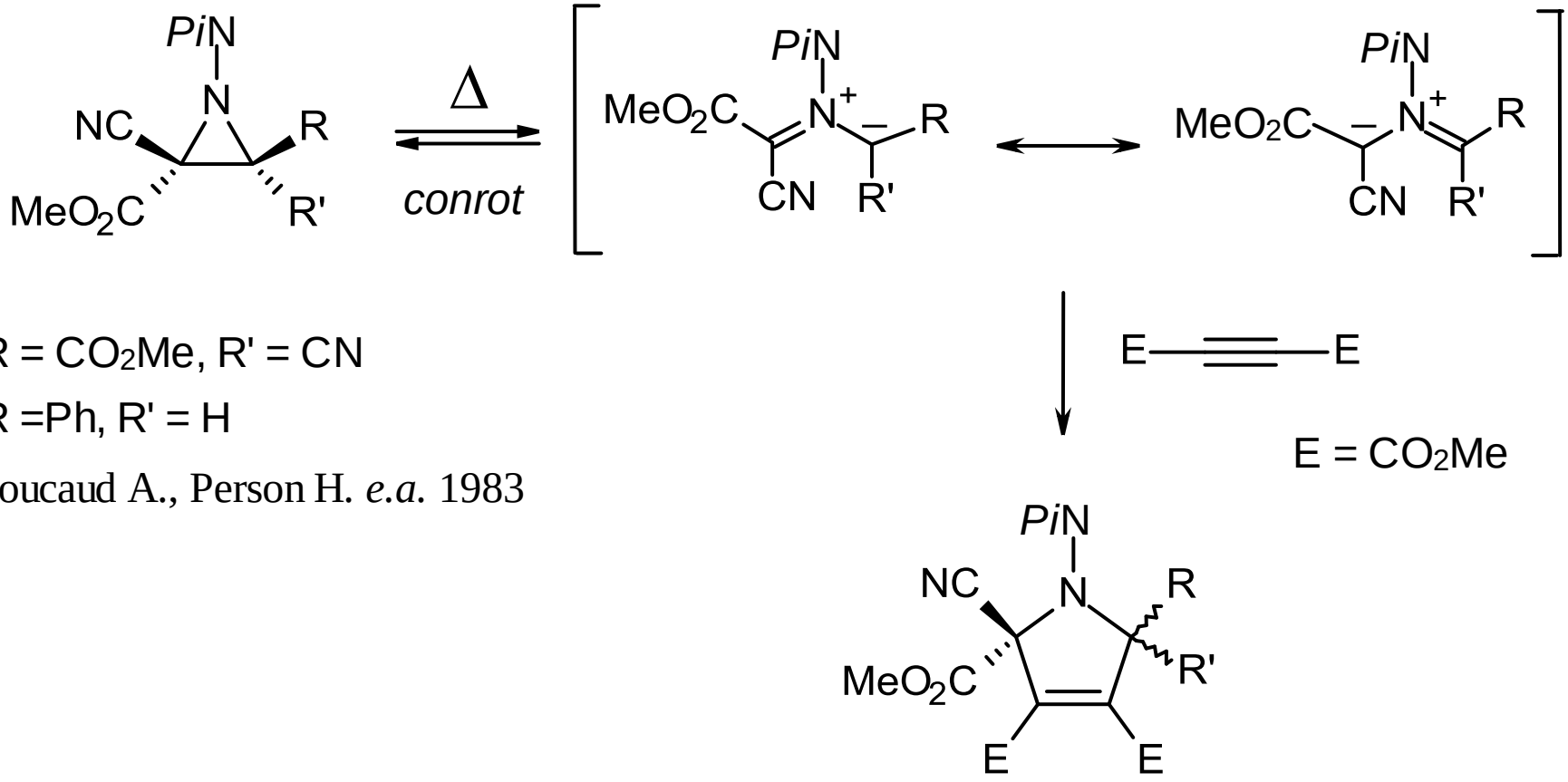


Asian J. Org. Chem. **2016**, *5*, 389-398

N-Фталимидоазометинилиды



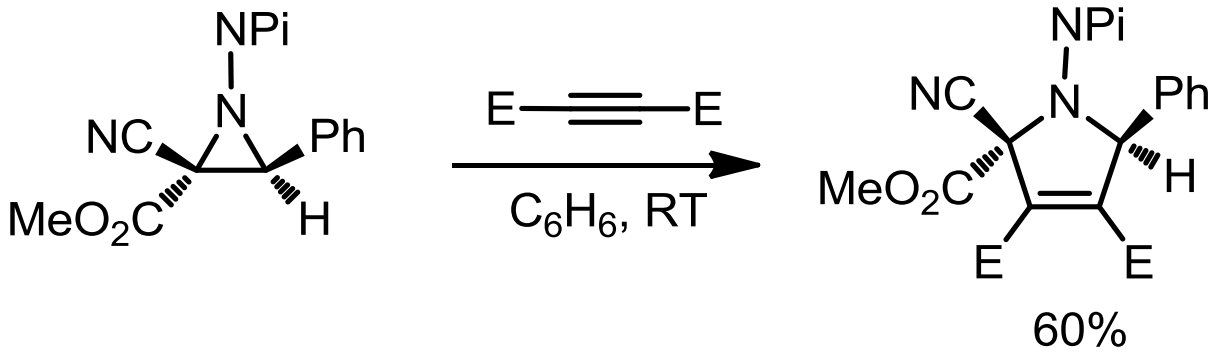
Литературные данные

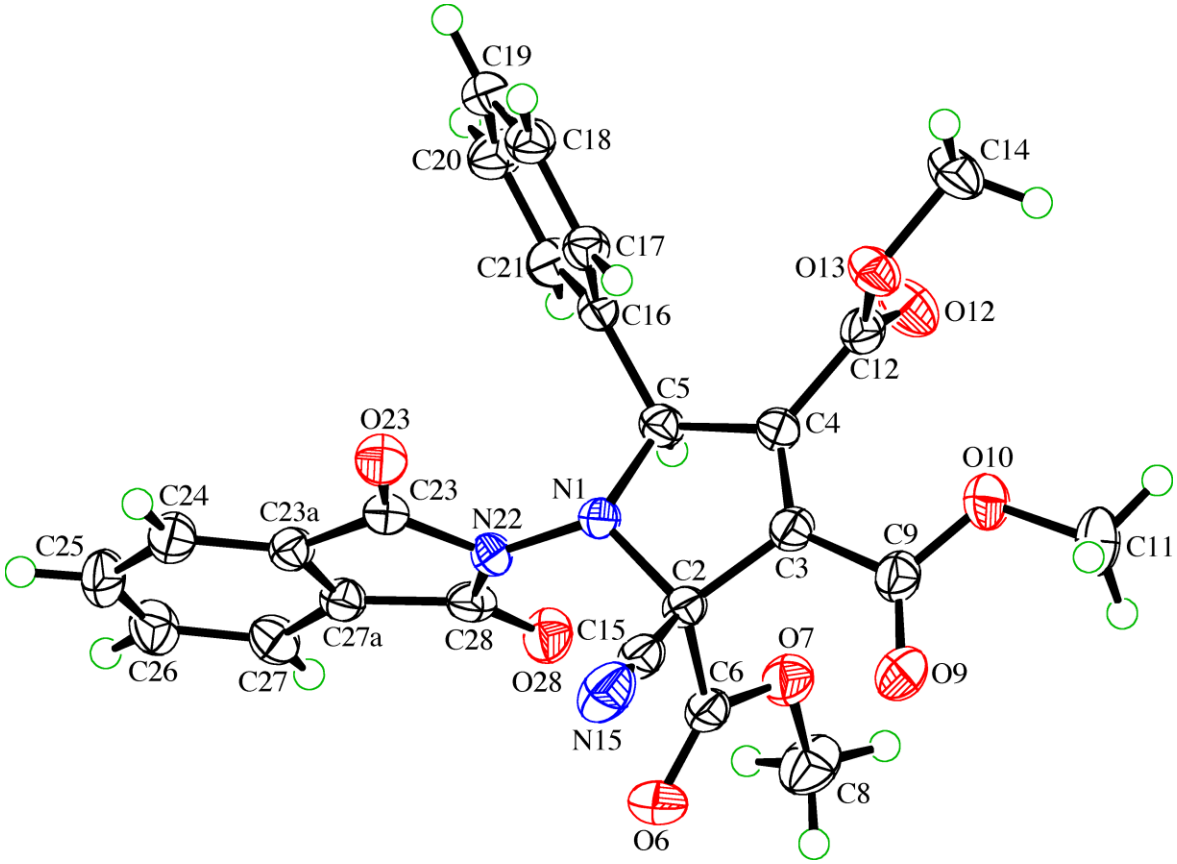


R = CO_2Me, R' = CN

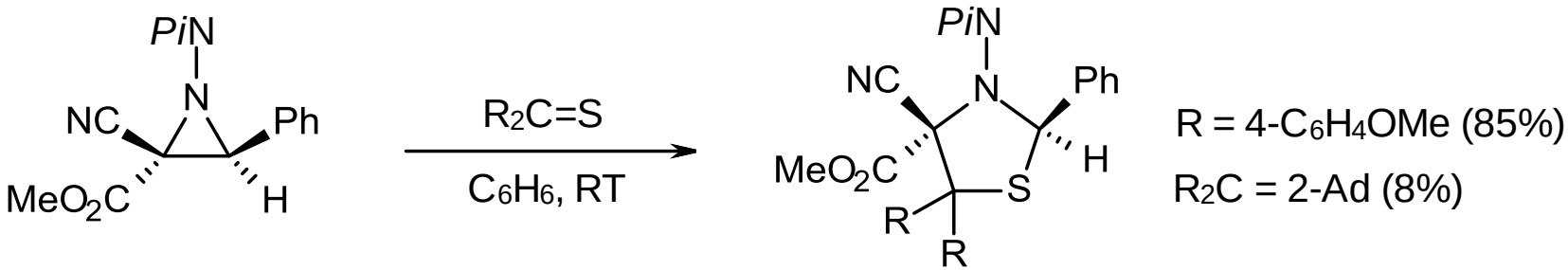
R =Ph, R' = H

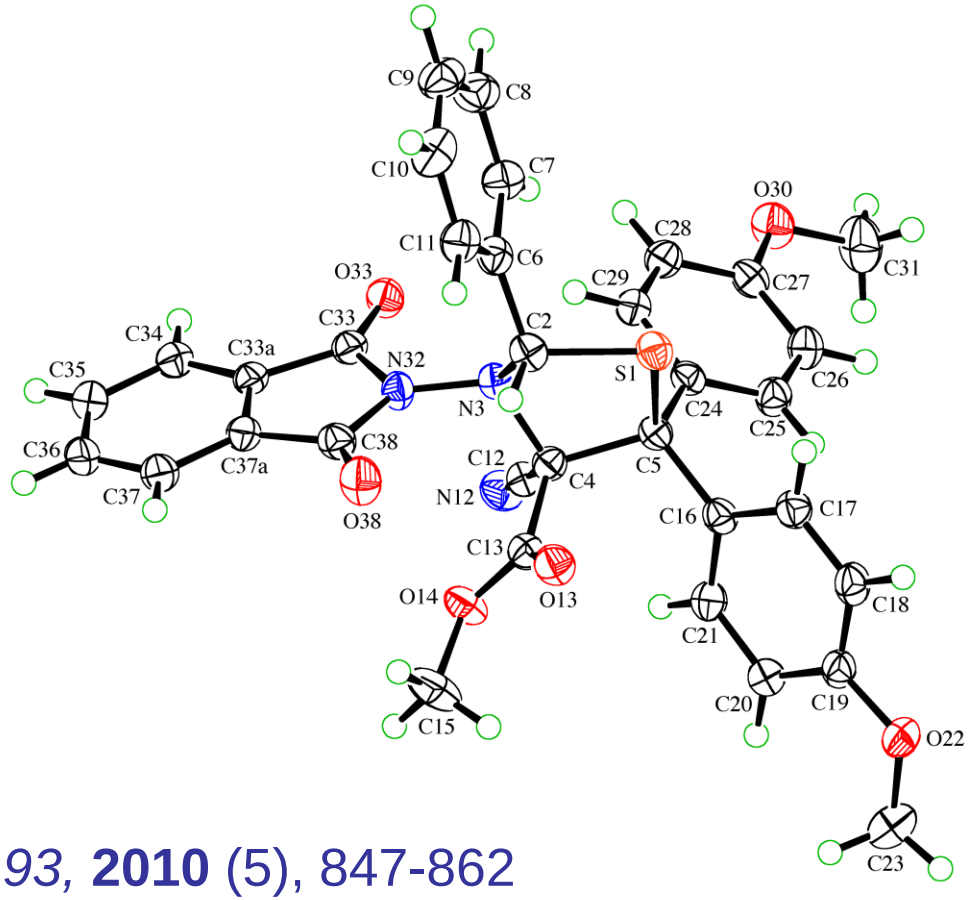
Foucaud A., Person H. *e.a.* 1983



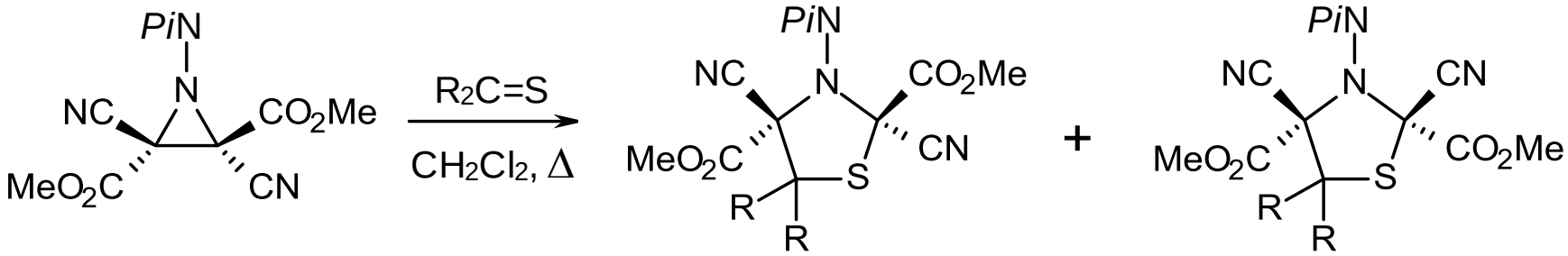


Helv.Chim.Acta, *93*, **2010** (5), 847-862



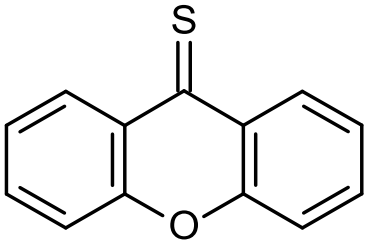


Helv.Chim.Acta, *93*, **2010** (5), 847-862



R = 4-C_6H_4OMe 31% 23%

$R_2C{=}S$ =

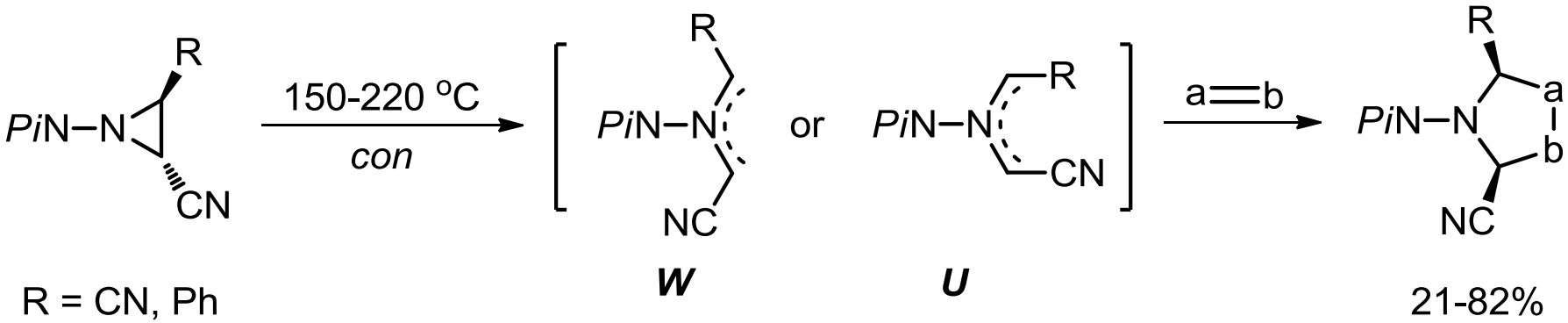


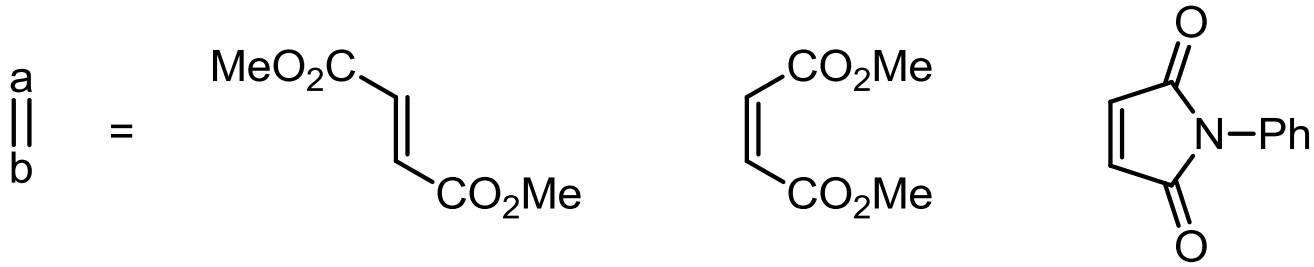
29% 12%

Structures of both *trans*-isomers were confirmed by X-ray data

Helv.Chim.Acta, *93,* **2010** (5), 847-862

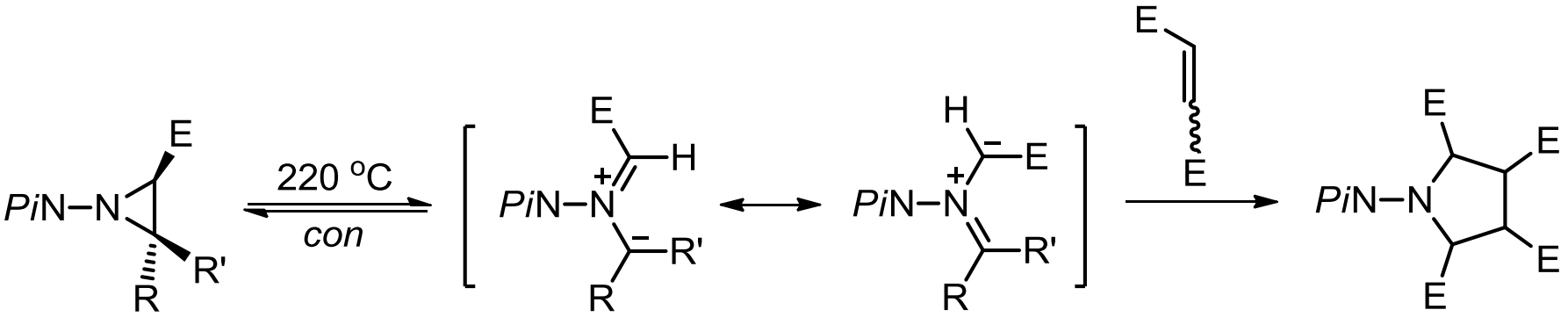
2,3-Дизамещённые азиридины





ЖОрХ, *44* (**2008**), N 12, 1807-1815 (Russ.); 1780-1788 (Engl.)

Стереохимия циклоприсоединения



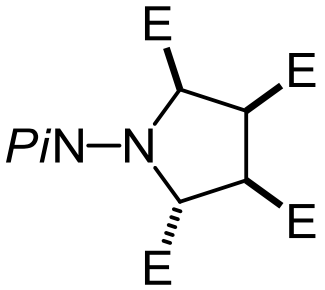
R = E, R' = H
R = H, R' = E
E = CO_2Me

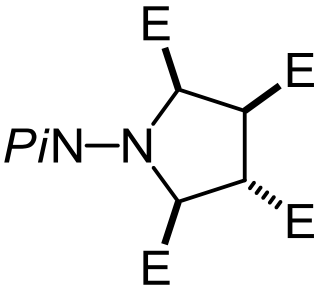
22-88%

Всего из 4 реакций выделено 5 стереоизомерных продуктов

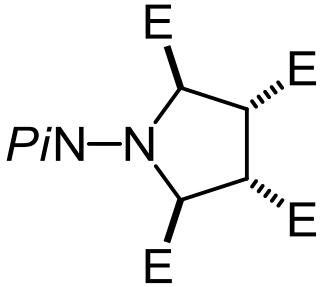
ЖОрХ, **45** (8), 1209-1216 (2009)

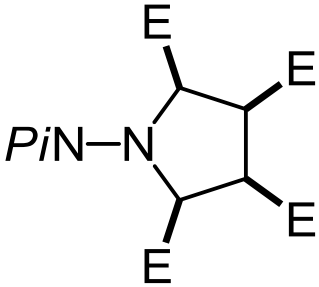
Варианты



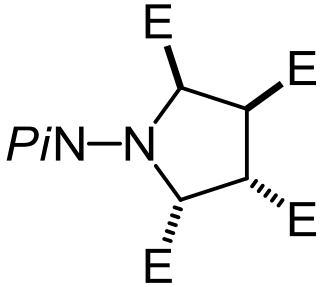


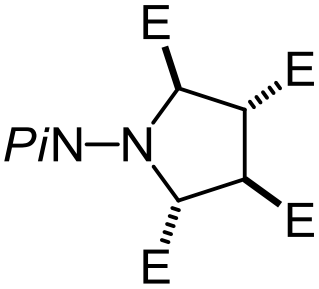
C_1 *ABXY*





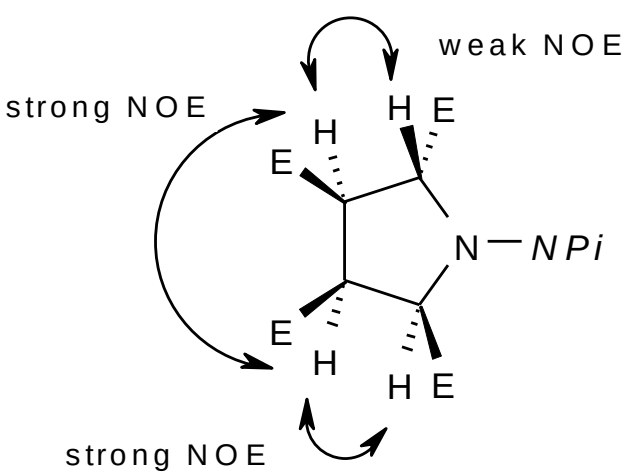
C_S *AA'XX'*

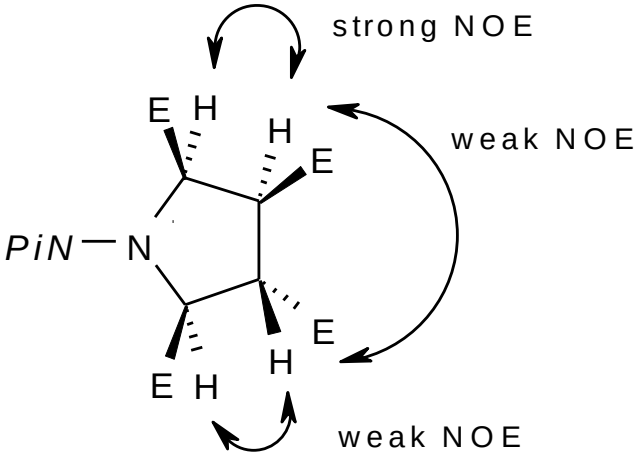




C_2 *AA'XX'*

Несимметричные продукты

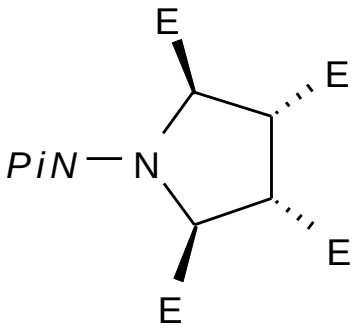


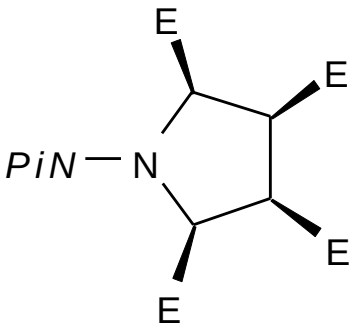


C_1 $ABXY$

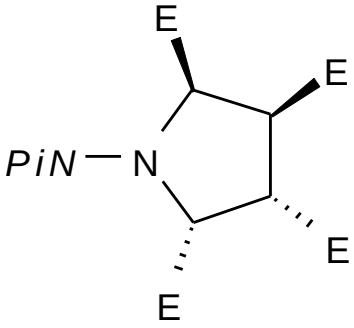
$J_{2,3} = J_{3,4} = J_{4,5} = 8.4$ Hz

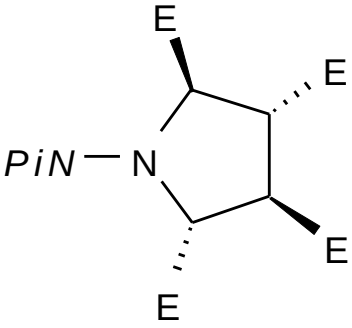
Что в остатке?





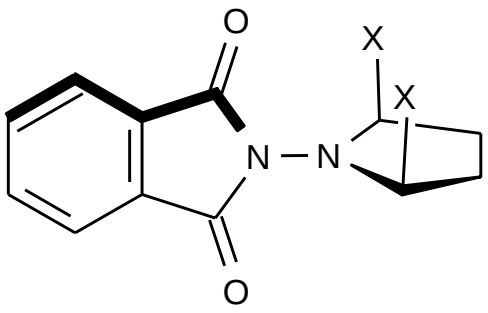
C_s $AA'XX'$





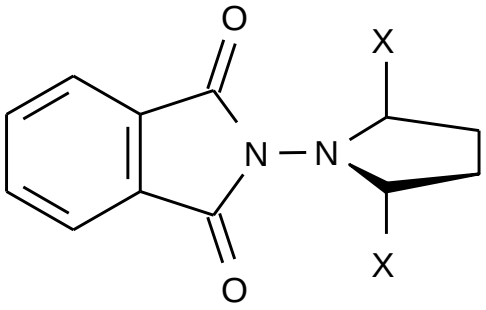
C_2 $AA'XX'$

Следствия замедления вращения по связи N-N



C_s

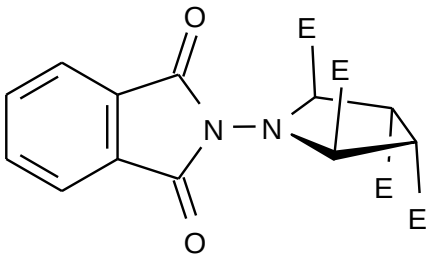
Две половины фталимидного заместителя при замедлении вращения по связи N-N становятся неэквивалентными

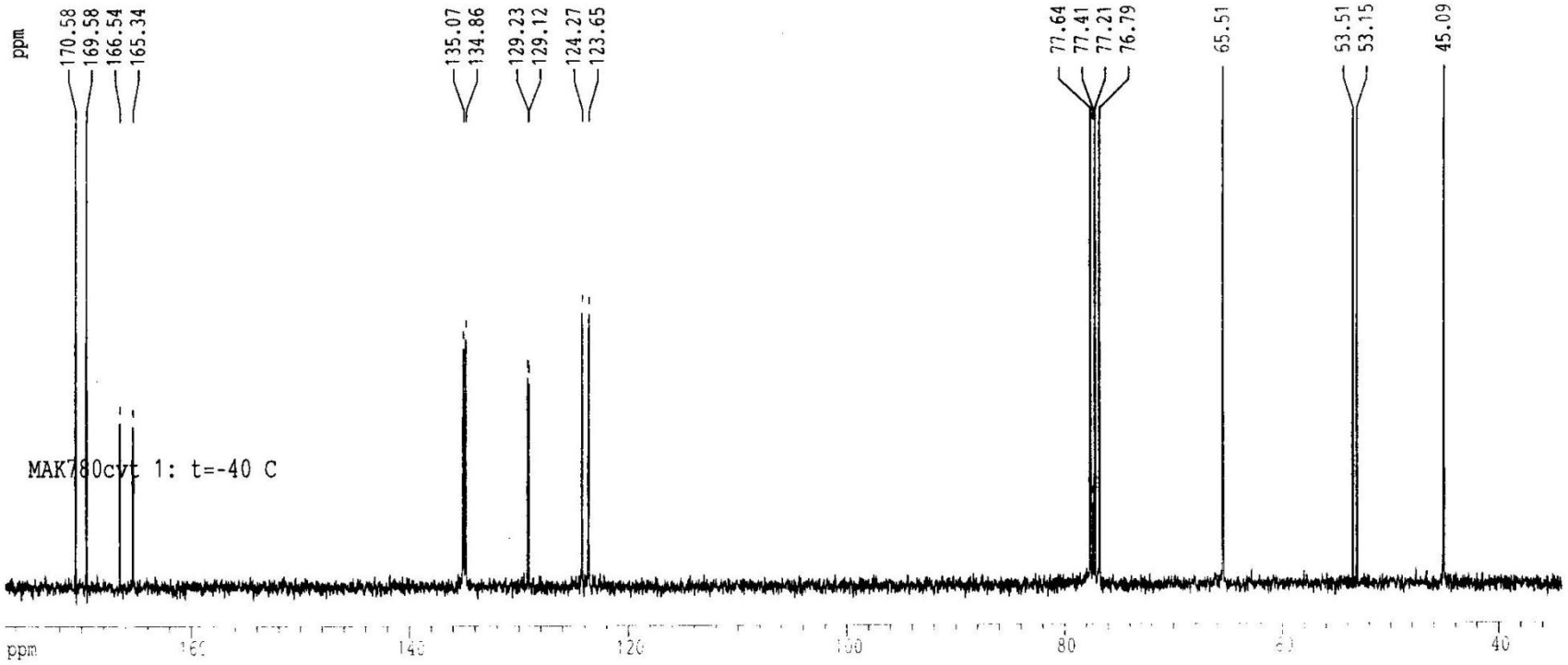


C_2

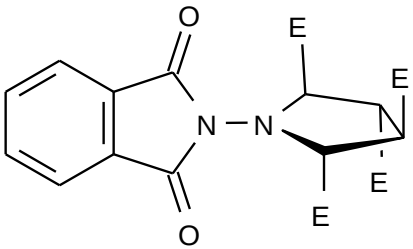
Две половины фталимидного заместителя эквивалентны при любой скорости вращения по связи N-N

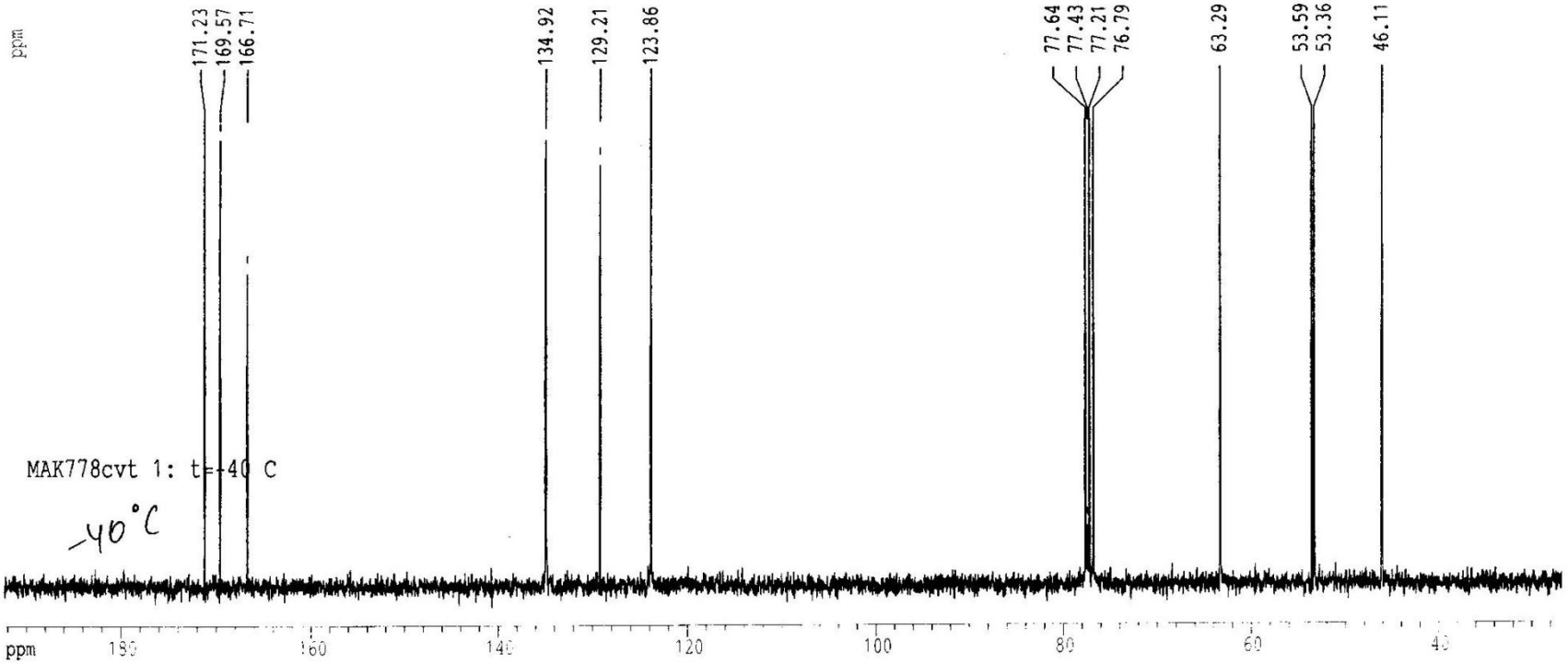
Спектр ЯМР ^{13}C аддукта C_s при -40°C



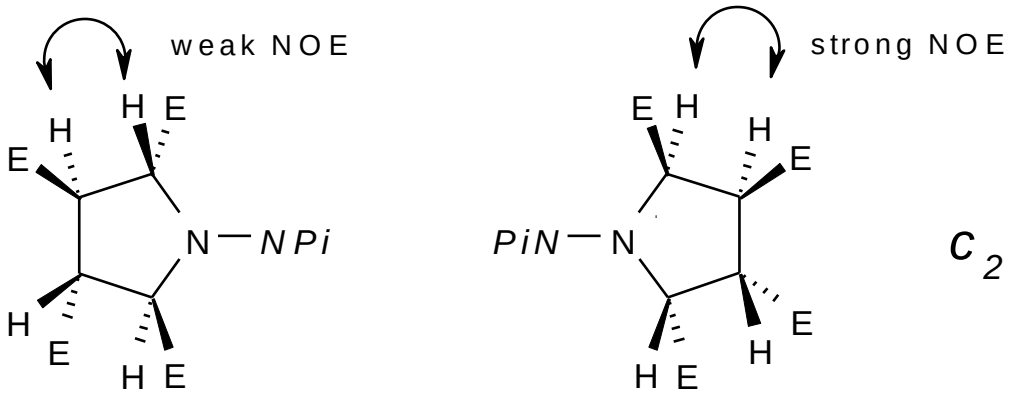


Спектр ЯМР ^{13}C аддукта C_2 при -40°C

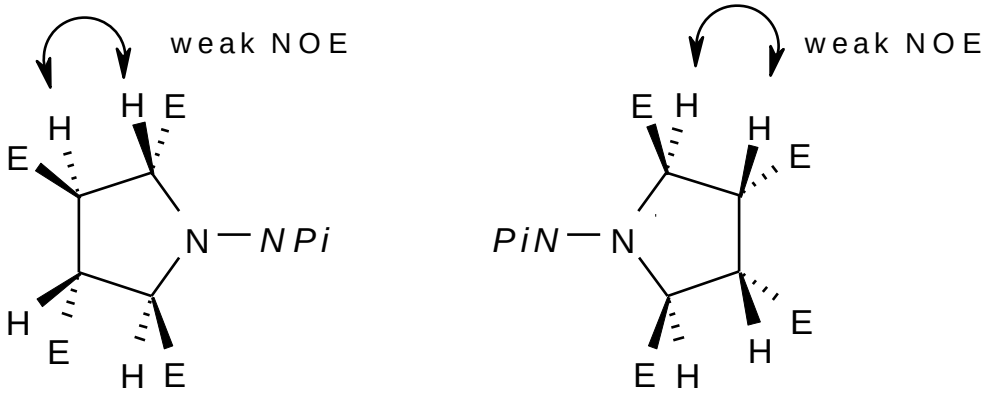




Различение симметричных продуктов

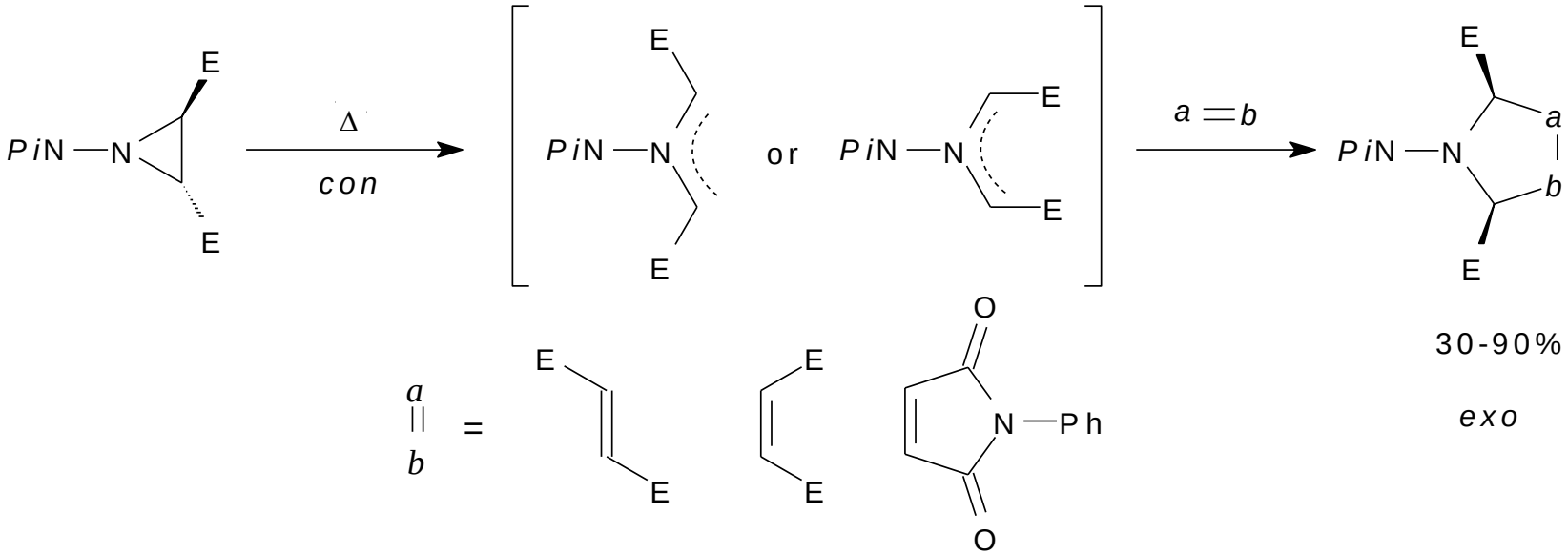


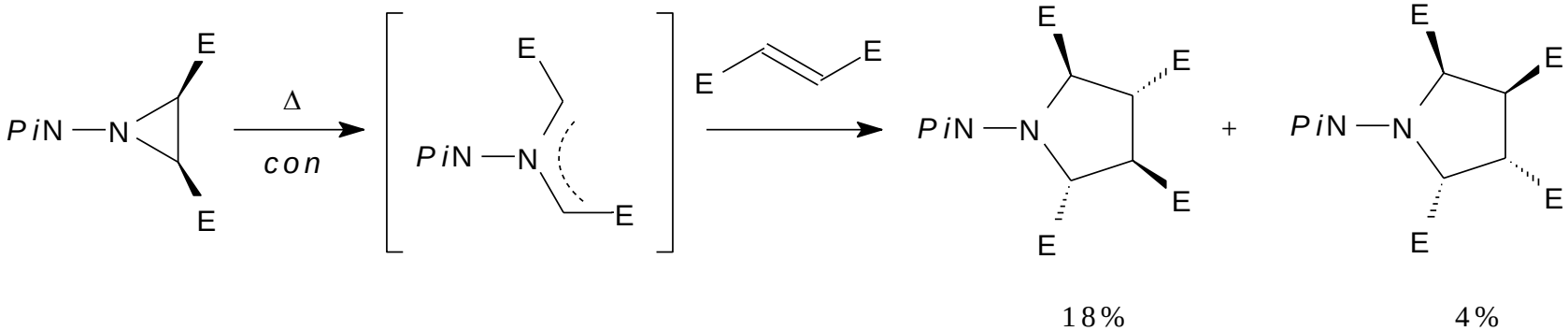
mixture 1:1



mixture 1:1

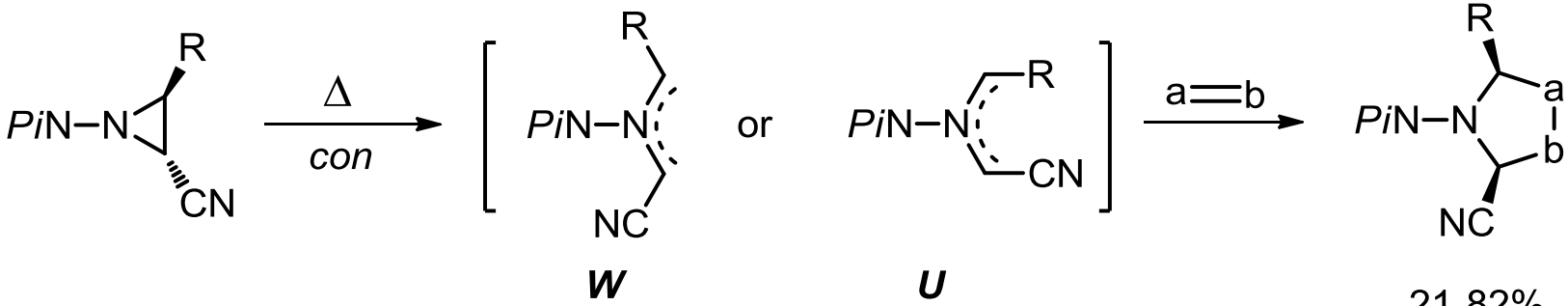
Стереоспецифичность и стереоселективность. Итог



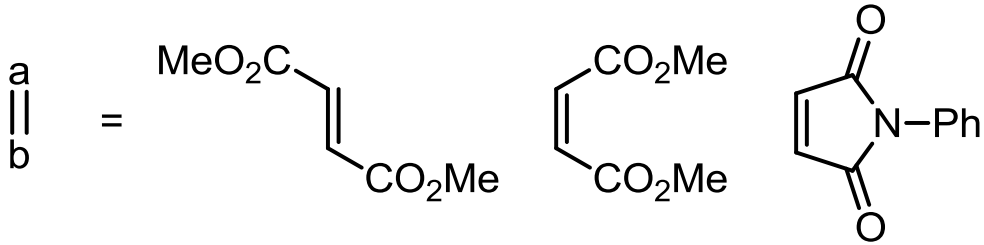


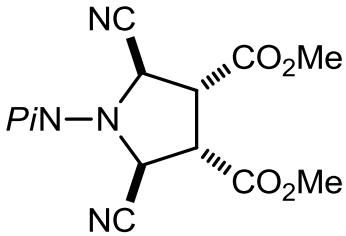
ЖОрХ, **45** (8), 1209-1216 (2009)

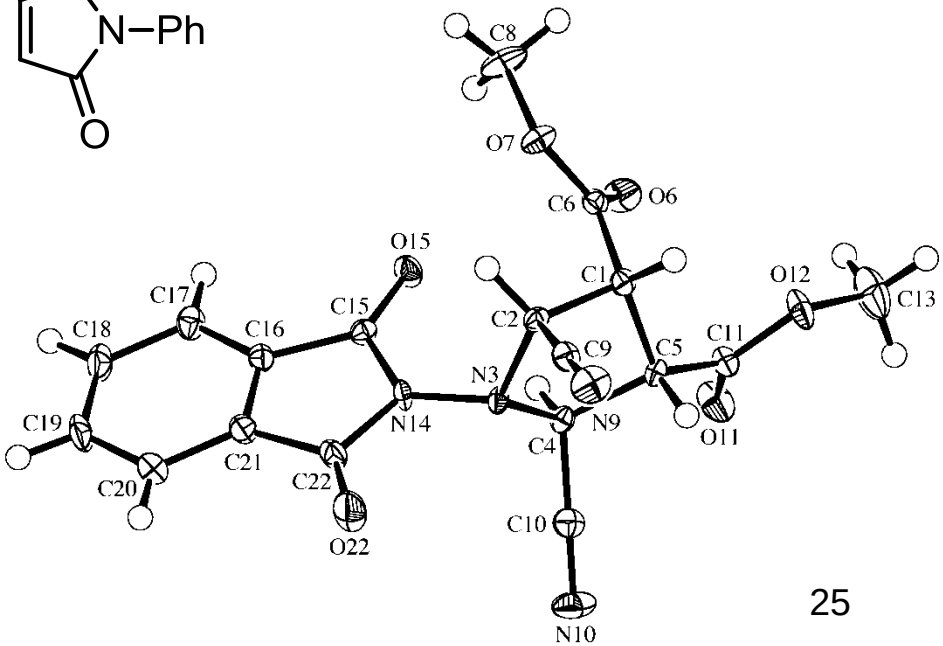
Другие фталимидоазиридины



R = CN (220 °C), Ph (150 °C)

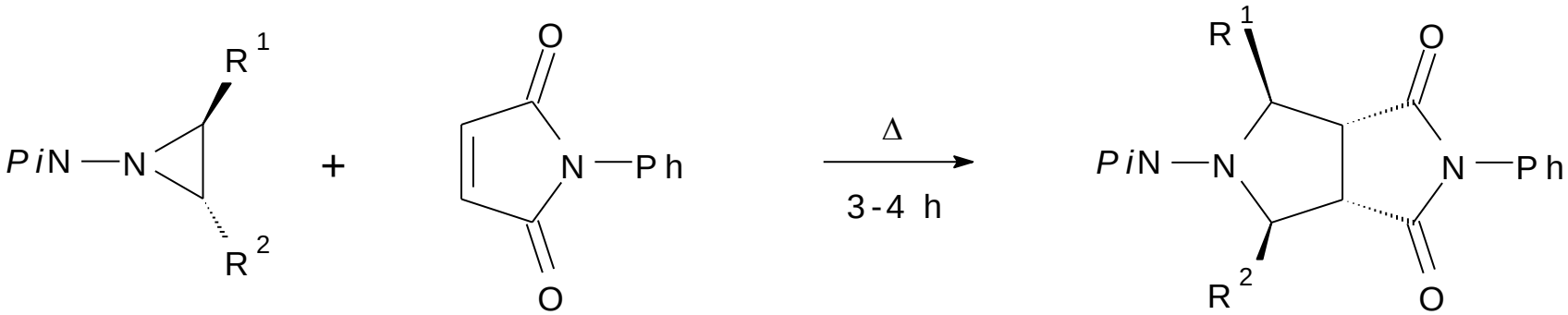






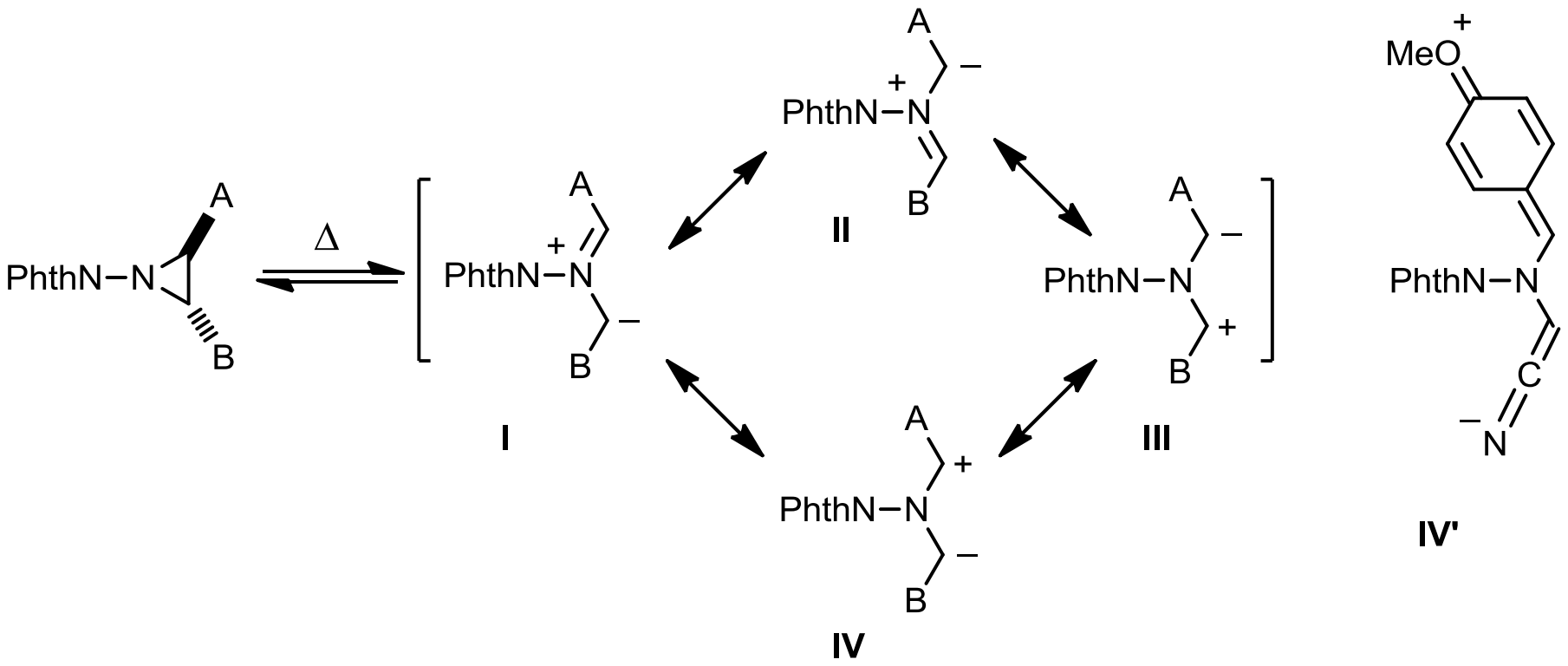
ЖОрХ, **44** (12), 1807-1815 (2008)

Электронные эффекты

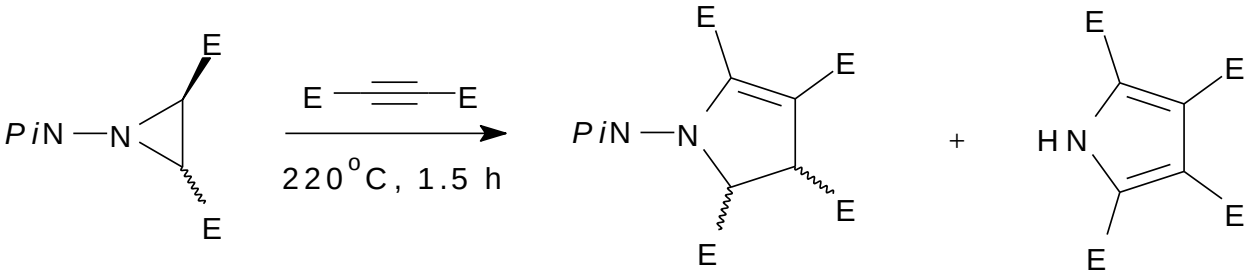


R^1	R^2		
E	E	220°C	88%
CN	CN	220°C	58%
Ph	CN	120°C	82%
$4\text{-}O_2NC_6H_4$	CN	135°C	89%
$4\text{-}MeOC_6H_4$	CN	115°C	69%
Ph	COOEt	150°C	69%
Ph	Ph	120°C	--

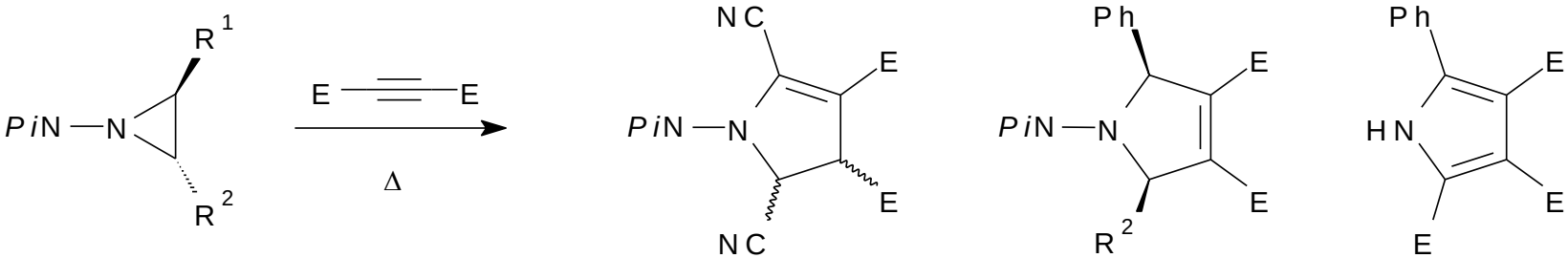
«Пуш-пулл»-замещение



Реакции с ДМАД



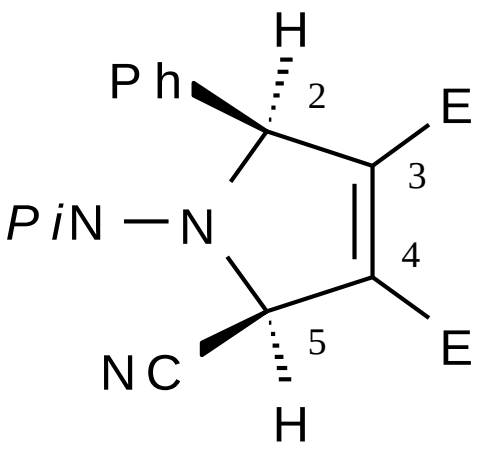
trans	-	50%
cis	20%	42%

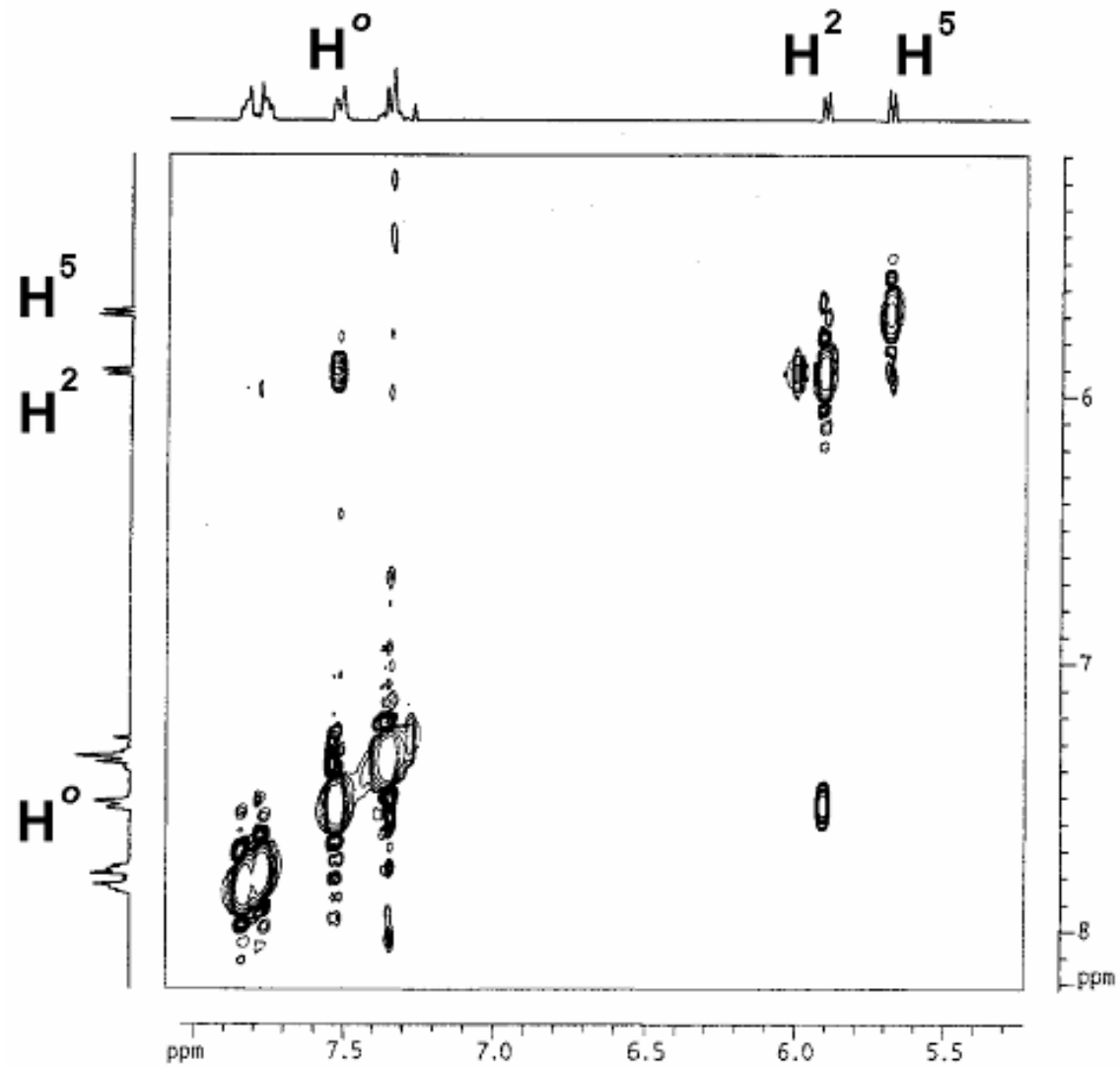


R^1	R^2				
				J (H^2-H^5) ~ 5 Гц	
CN	CN	150°C, 1.5 h	33%		
Ph	CN	120°C, 2 h		77%	
Ph	E	150°C, 3.5 h		32%	21%

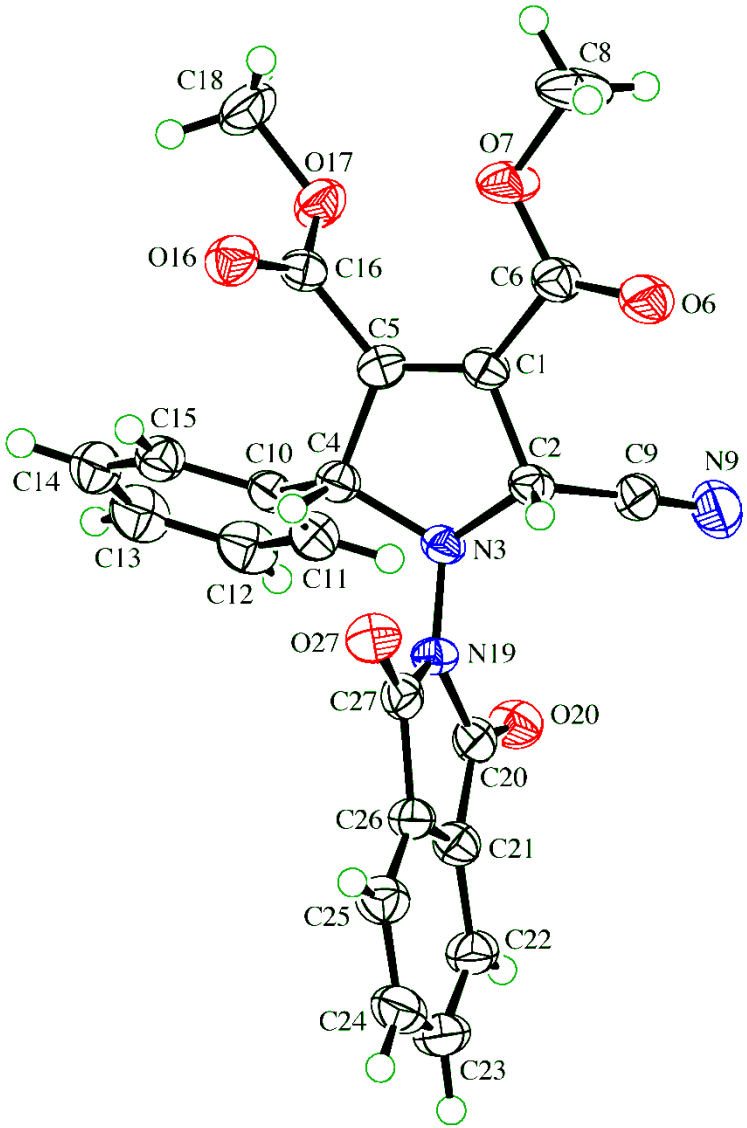
Вестник СПбГУ, Сер. 4. **2009.** вып. 1, с. 150-154

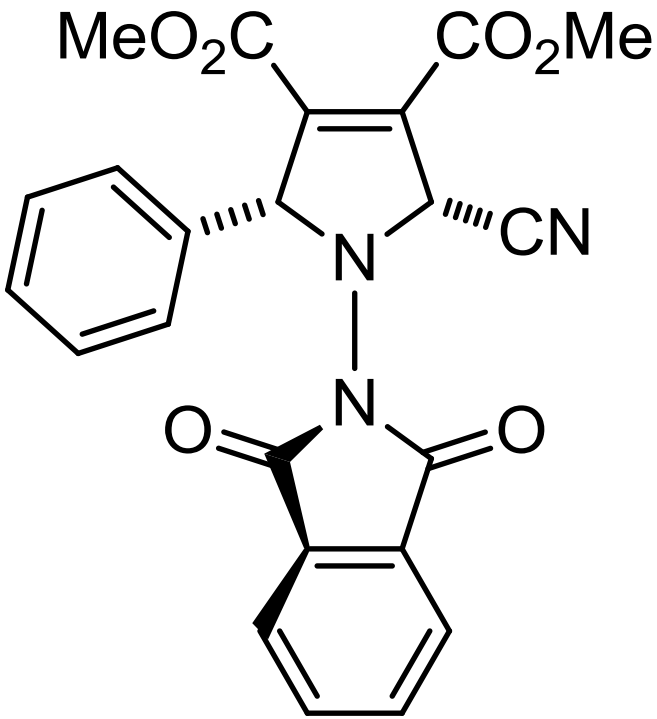
Спектр NOESY пирролина



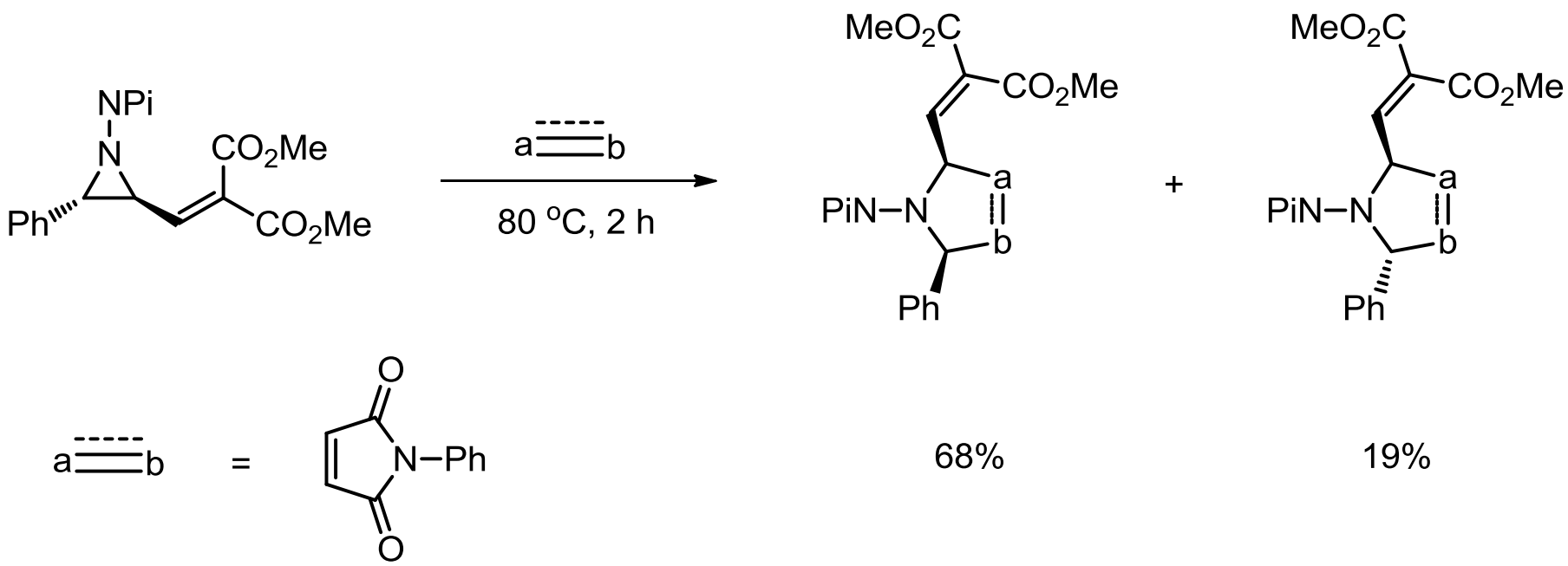


$\delta(C^3) = 147$ ppm
$\delta(C^4) = 124.6$ ppm


C18
C8
O17
O7
O16
C16
C6
O6
C5
C1
C15
C10
C4
C2
C9
N9
C14
C13
C12
C11
N3
O27
N19
C27
O20
C20
C26
C21
C25
C22
C24
C23

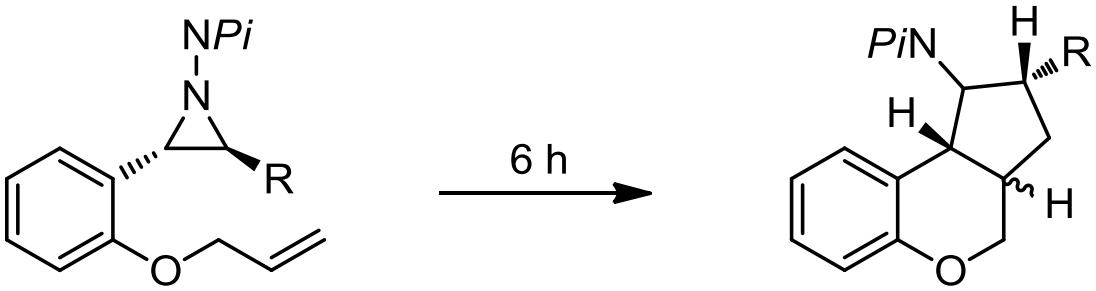

MeO2C
CO2Me
CN
N
N
O
O

НО!

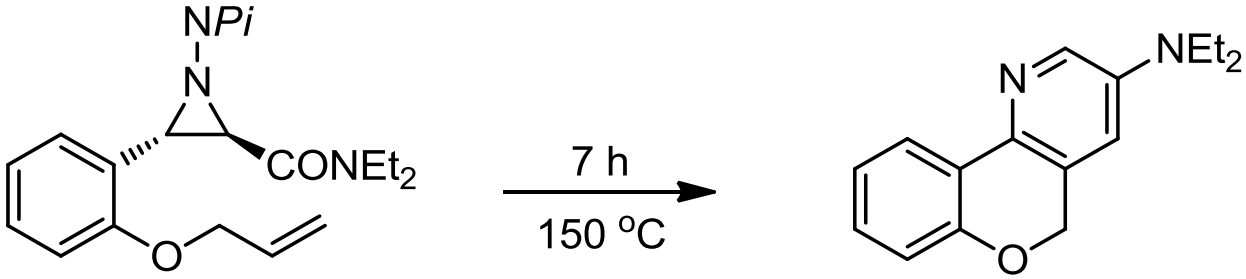


ЖОрХ., *49* (**2013**), N 1, 91-100 (Russ.); 83-94 (Engl.)

Внутримолекулярное циклоприсоединение



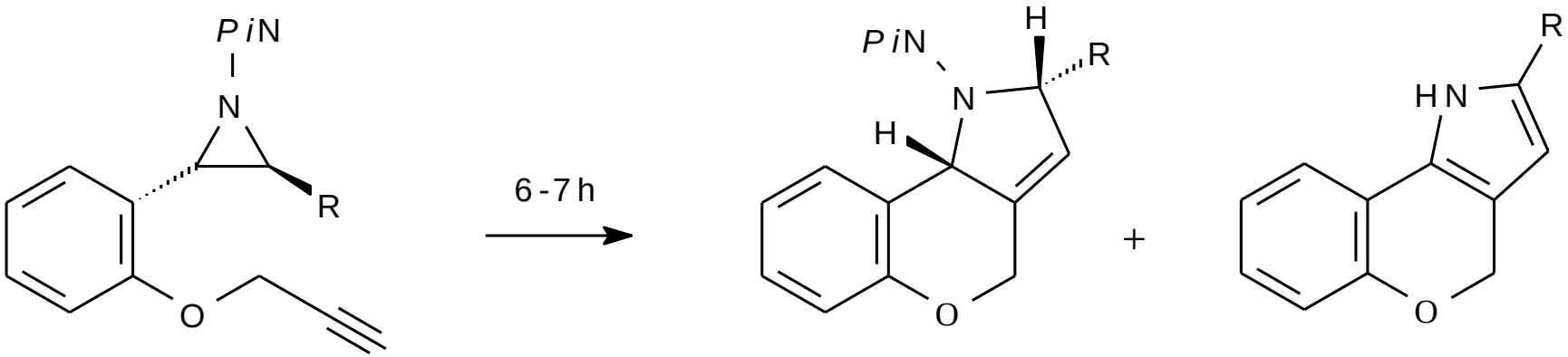
R = CO_2Me	150 °C	10% *cis* : *trans* = 2.3 : 1
R = CN	120 °C	50% *cis* : *trans* = 2 : 1



13%

Tetrahedron Lett., *50,* **2009** (44), 5990-5993

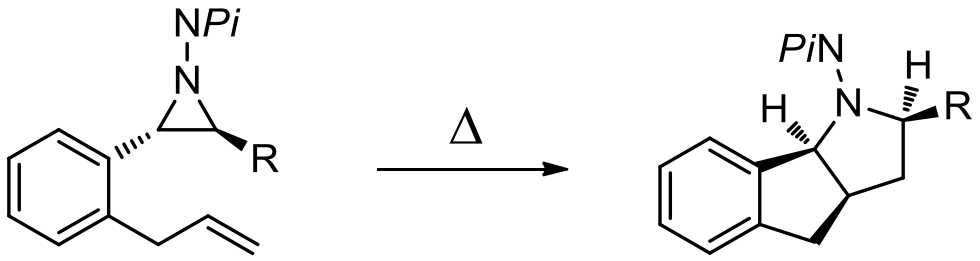
И по связи C≡C



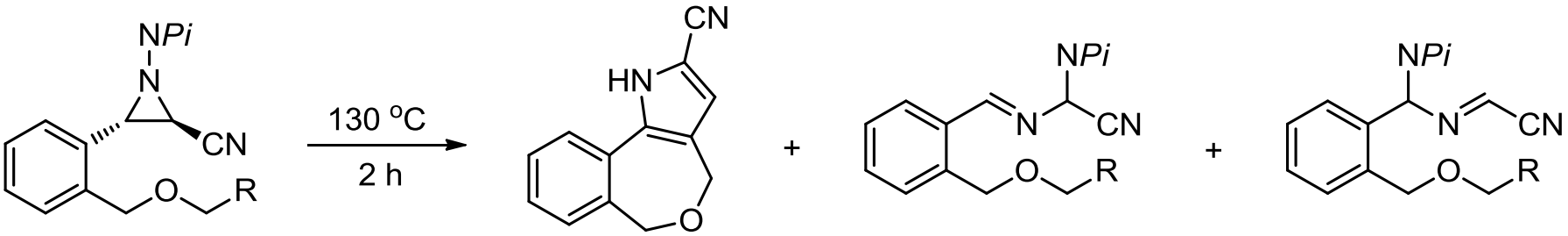
R = COOMe	150°C	53%	9%
R = CN	120°C	91%	-
R = CONEt$_2$	150°C	11%	11%

Tetrahedron Lett., *50,* **2009** (44), 5990-5993

Замыкание 5- и 7-членных циклов



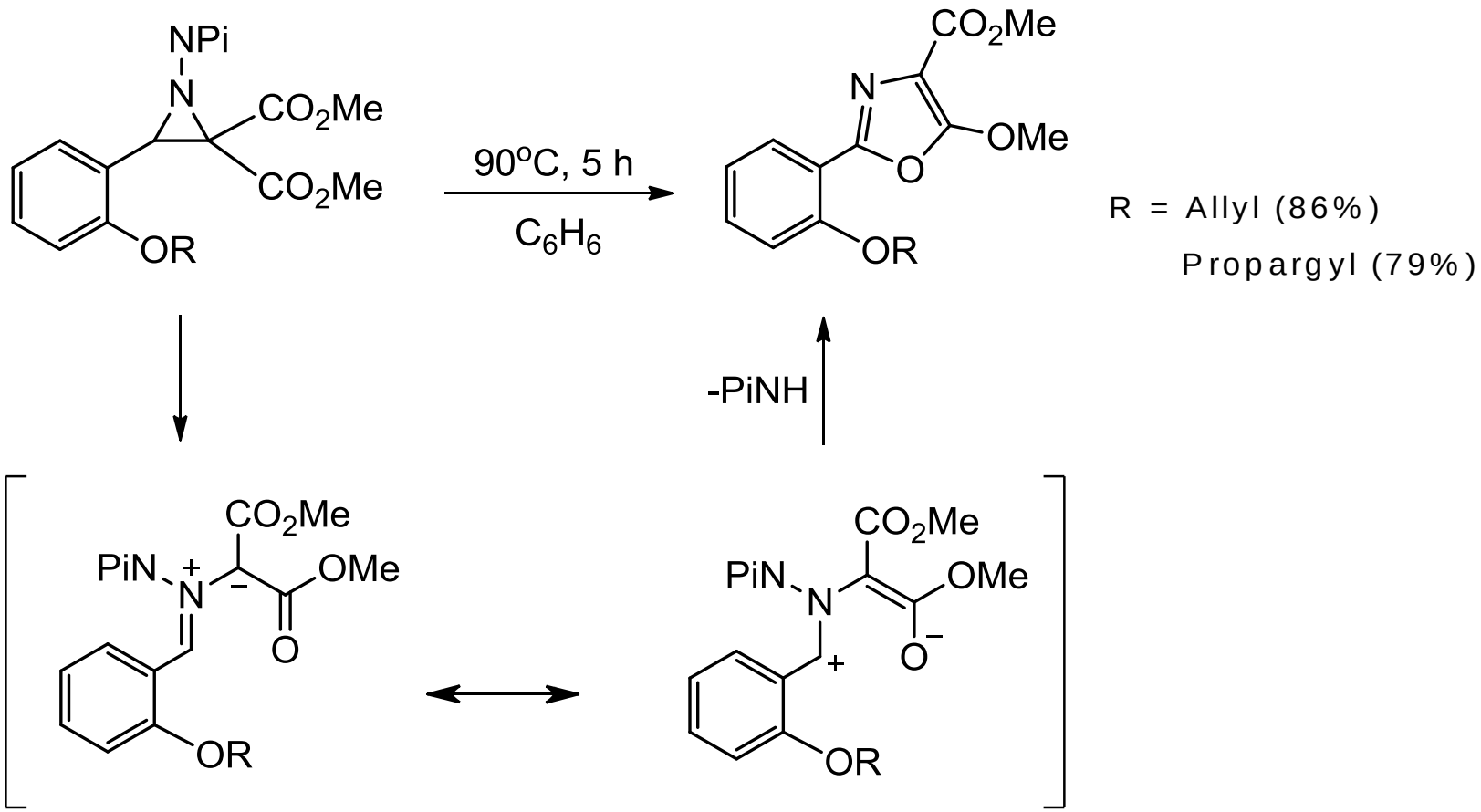
R = CO_2Me	150 °C, 3 h	59%
R = CN	120 °C, 2.5 h	70%



R = —C≡CH	22%	24%	19%
R = —CH=CH_2		23%	16%

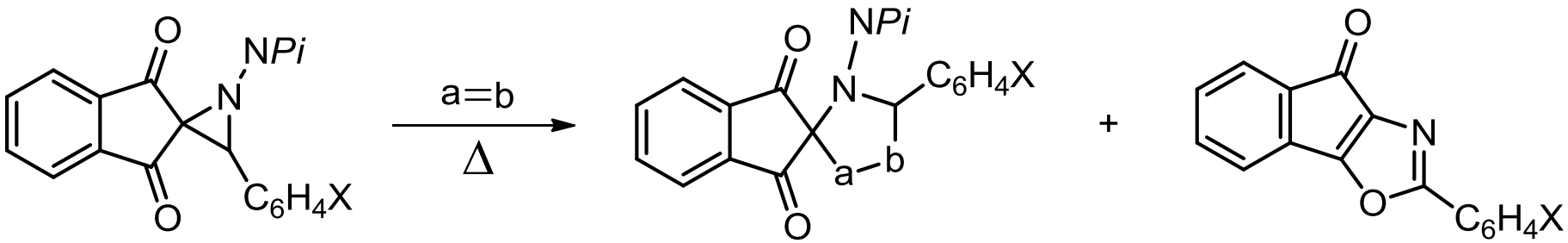
Chem. Heterocyclic Compd. (*Khim. Get. Soed.*), *47* (**2011**), N 11, 1353-1366 (Engl); 1632-1648 (Russ.)

Превращение в 1,3-оксазолы



Tetrahedron Lett., *50,* **2009** (44), 5990-5993

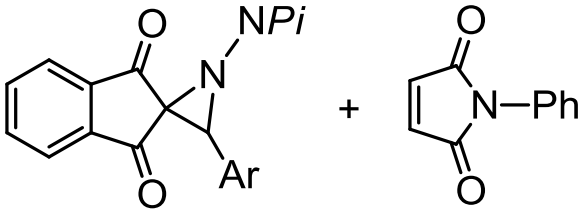
Спироазиридины. Конкуренция двух процессов



p-X		PhMI	DMAD	*Z*-	*E*-
NO_2	75 °C, 8 h	87 / 0	66 / 5	25 / 30	0 / 60
Cl	55 °C, 9 h	95 / 0	77 / 14	0 / 28	0 / 37
Me	25 °C	35 / 0	0 / 0	0 / 0	0 / 0

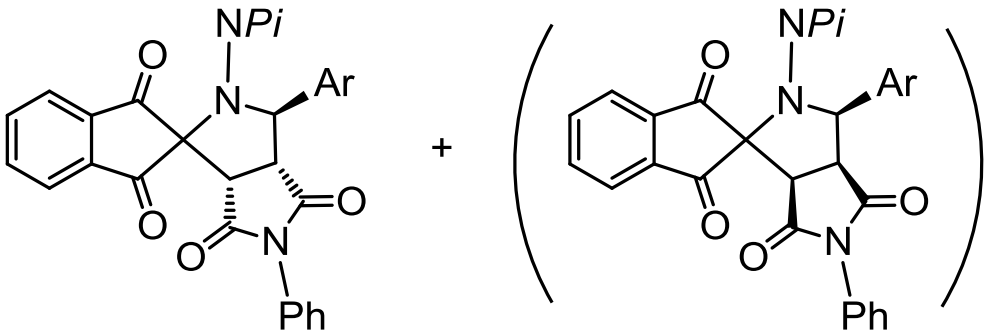
Tetrahedron Lett., *55*, **2014** (15), 2499-2503.

Циклоприсоединение спироазиридинов



MW or Δ
75 °C, C_6H_6

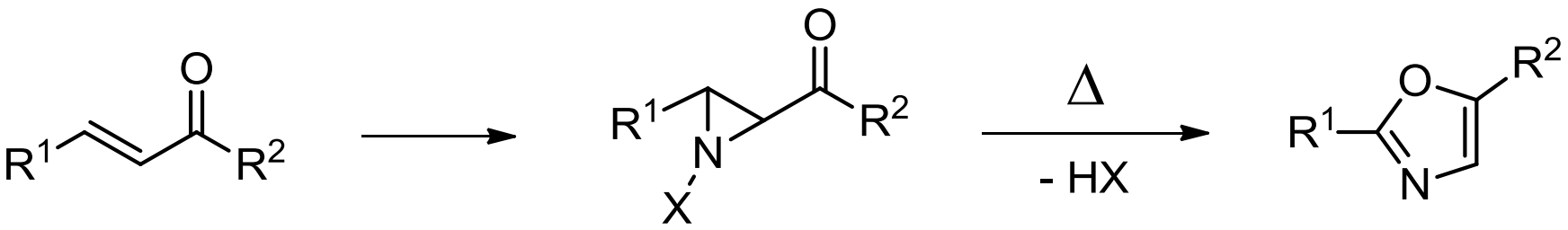
Ar = 4-$MeO_2CC_6H_4$ (**a**), 4-NCC_6H_4 (**b**),
4-$F_3CC_6H_4$ (**c**), 3-pyridyl (**d**)



a, *exo/endo*, 1:0.03, 71%,
b, *exo/endo*, 1:0.04, 78%,
c, *exo,* 88%,
d, *exo,* 75%

Tetrahedron Lett., *55,* **2014** (15), 2499-2503

Оксазолы из α,β-непредельных кетонов

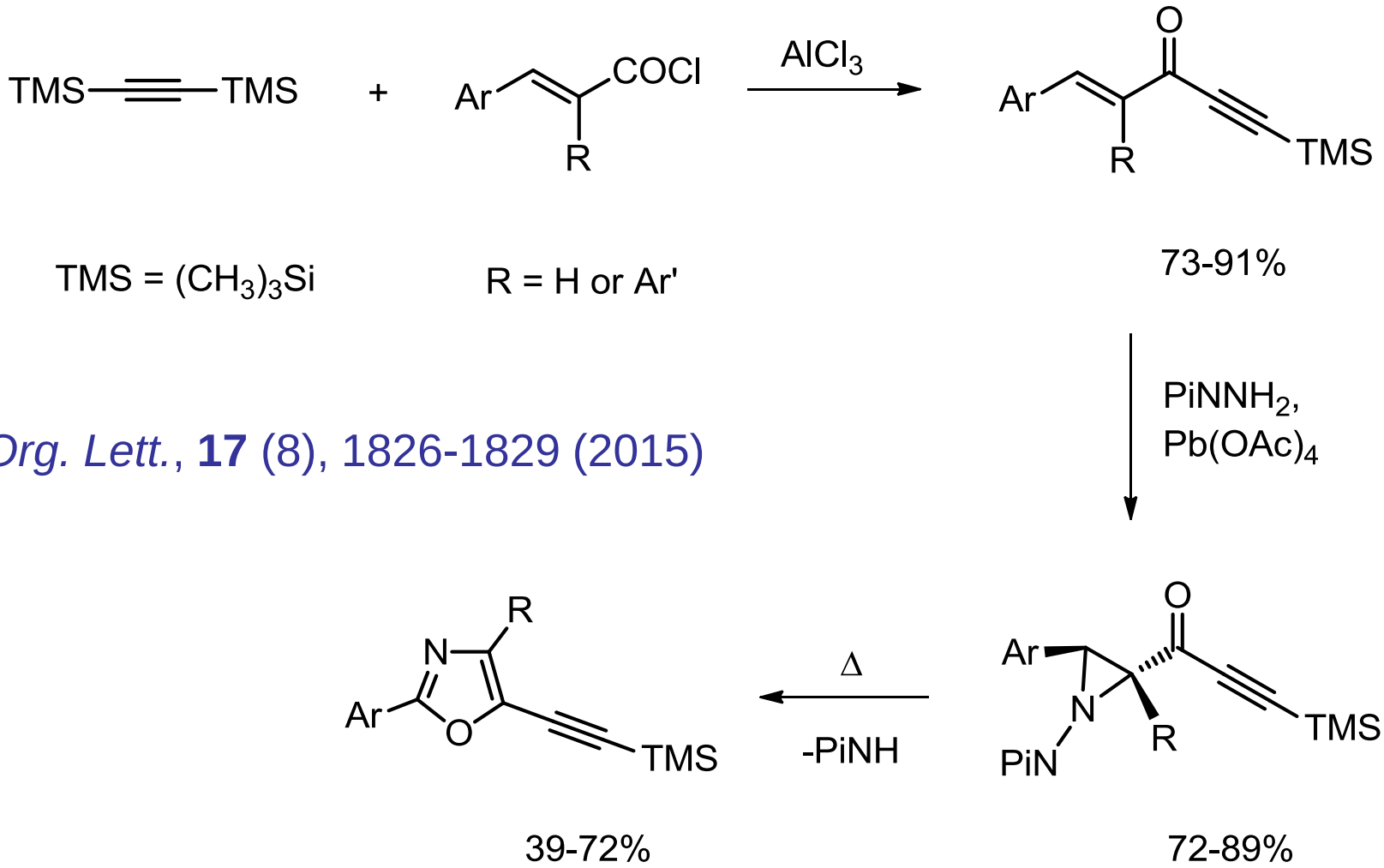


X = PiN, $PhSO_2$
R^1, R^2 = Ar, Alk

Yields are 20-50% for two steps

ЖОрХ, *45* (**2009**), N 8, 1237-1248 (Russ.); 1229-1240 (Engl).

Синтез 5-этинилоксазолов

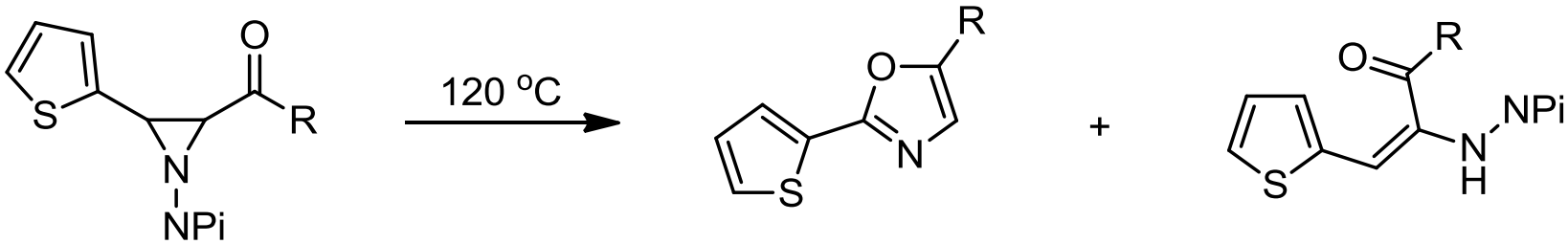


TMS = $(CH_3)_3Si$

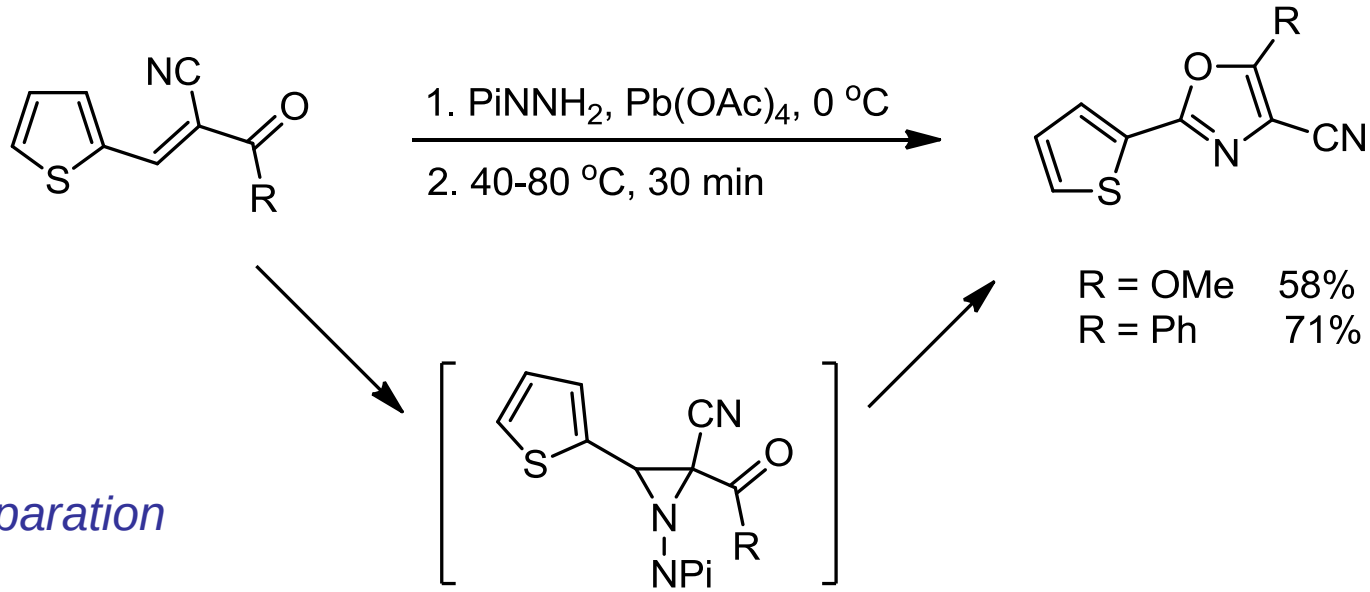
R = H or Ar'

Org. Lett., **17** (8), 1826-1829 (2015)

Синтез 2-тиенилоксазолов



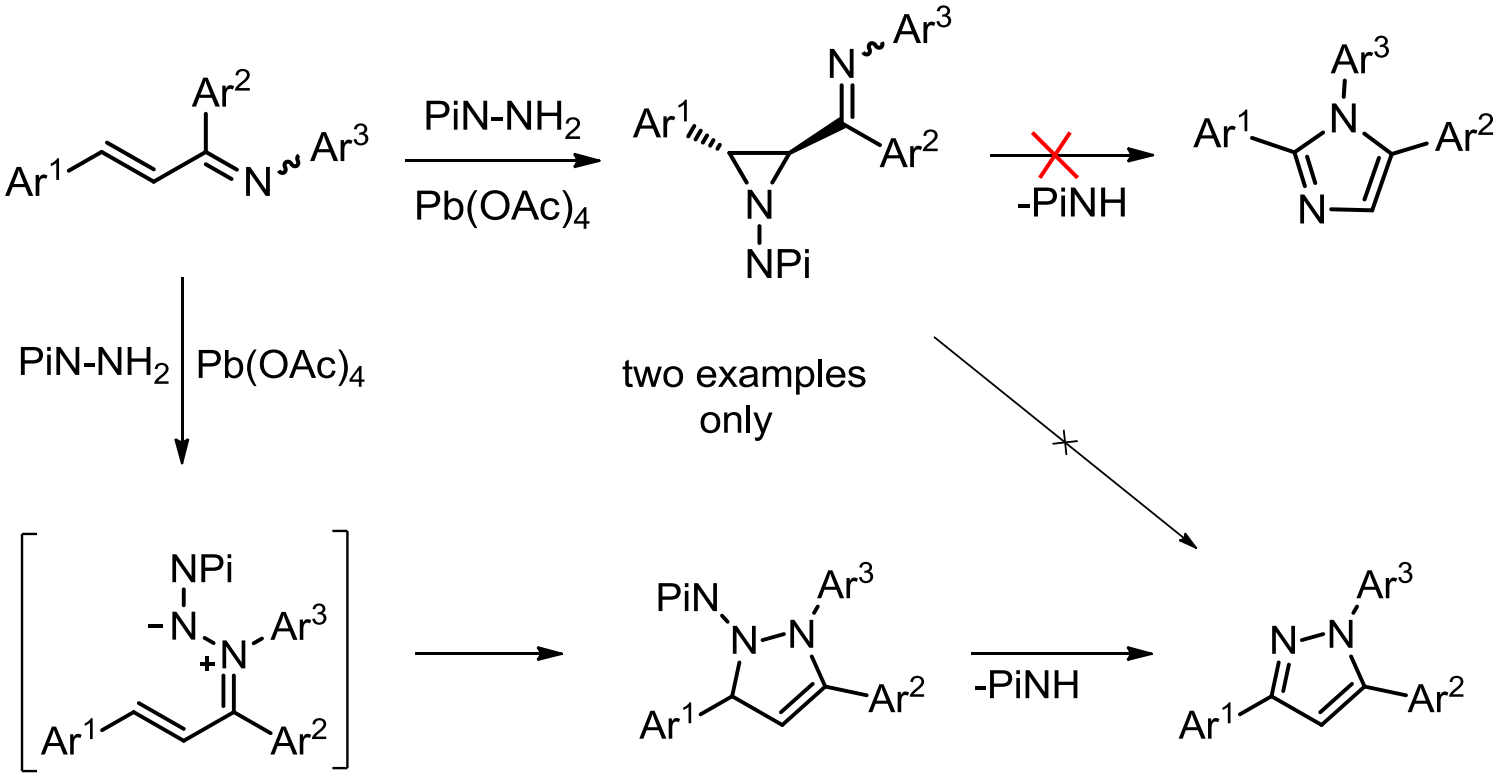
R = Me, Ph, —≡—TMS	30-55%	13-45%
R = OMe	–	66%



R = OMe 58%
R = Ph 71%

In preparation

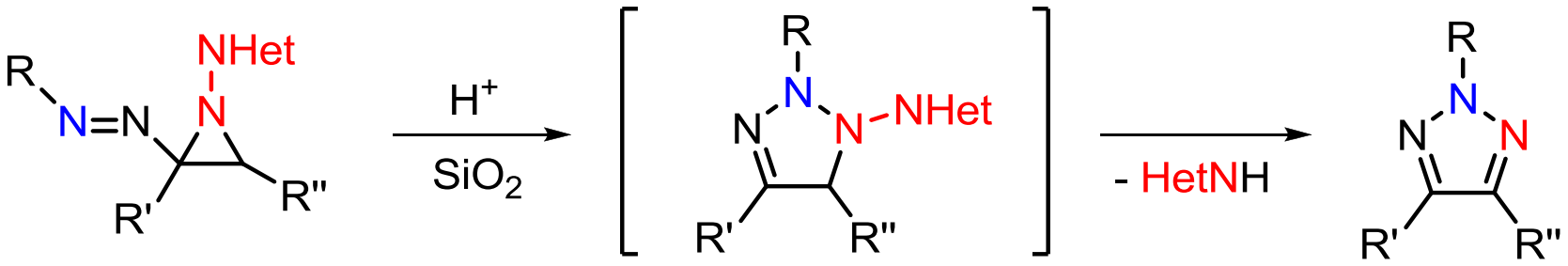
Превращения арилиминов халконов



Chemical Communications, submitted

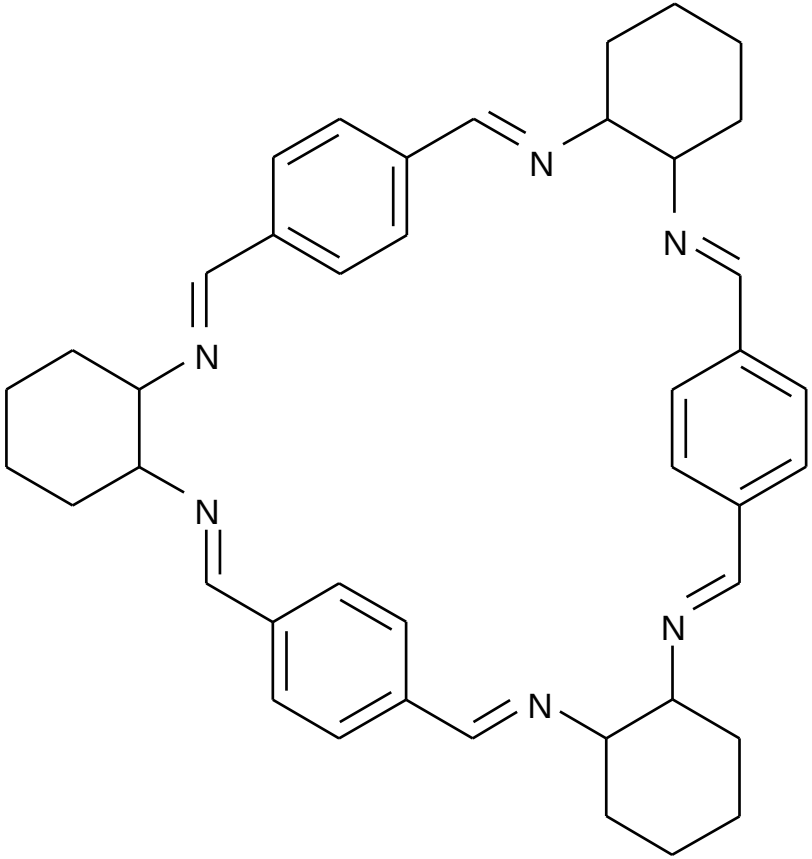
12 примеров
50-75%

Превращение азоазиридинов в 1,2,3-триазолы

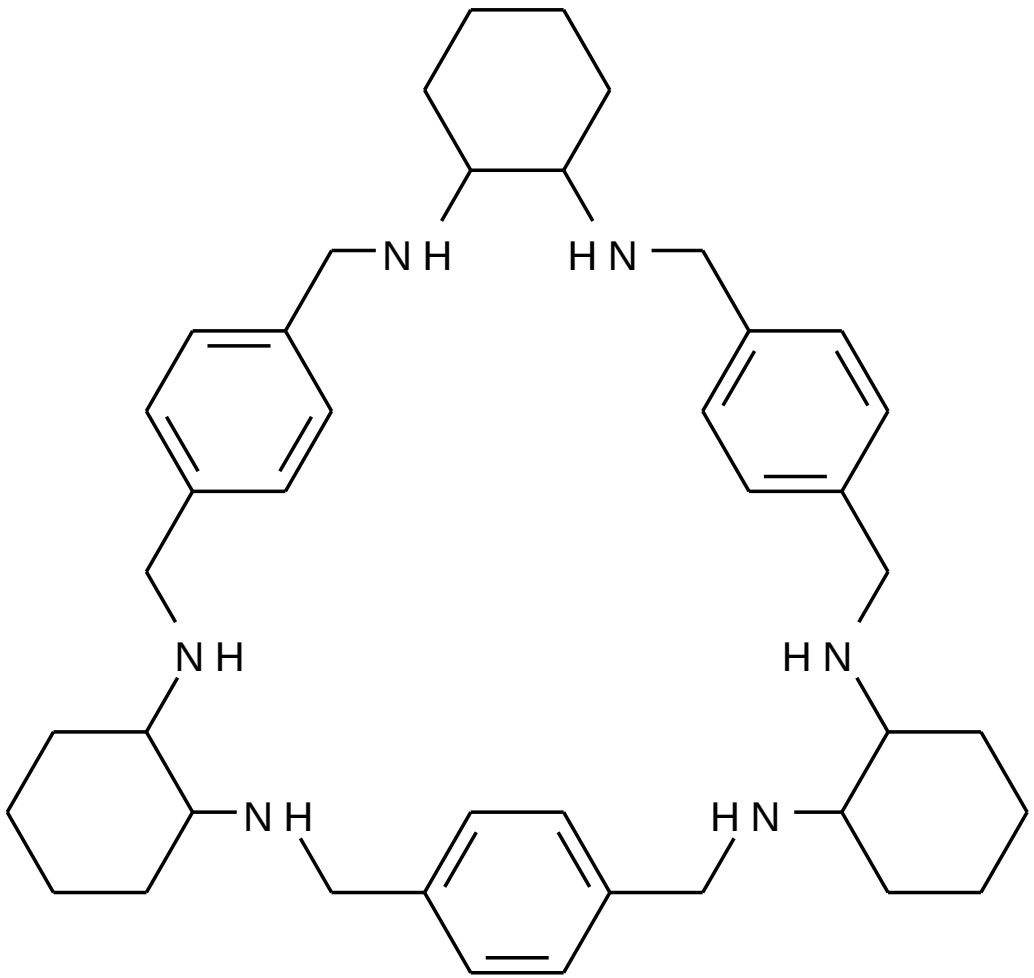


Eur.J.Org.Chem., **2001** (7), 1309–1314.
ХГС, *40* (**2004**), N 7, 868-870 (Engl.); 1043-1052 (Russ.);
41 (**2005**), N 10, 1321-1326 (Engl.); 1573-1578 (Russ.)

При конденсации *транс*-циклогексан-1,2-диамина с бензол-1,4-дикарбальдегидом с выходом более 90% образуется показанный ниже аддукт 3:3.



Затем его иминогруппы восстанавливают до аминных:



Вопрос: сколько и каких сигналов должно наблюдаться в протонном спектре продукта? В его углеродном спектре? И почему?

Благодарности

Dr. Е.В. Белецкий
К.х.н. А.В. Ушков
К.х.н. В.В. Воронин

Аспирант А.Ю. Стукалов

Грант РНФ №14-13-00126

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Institute of Chemistry

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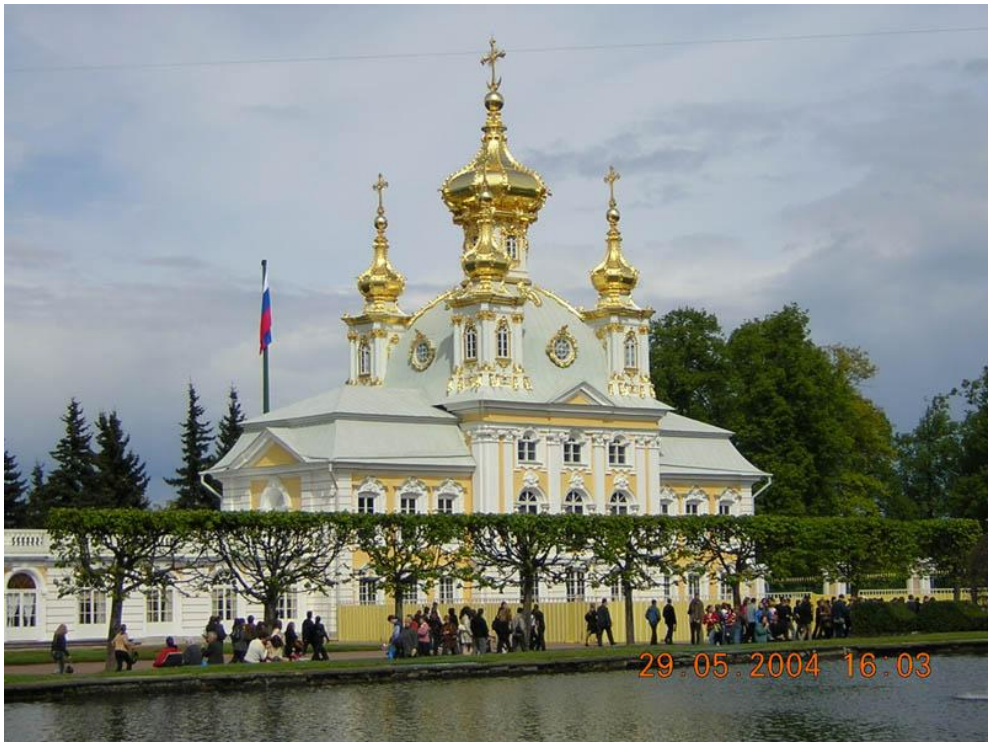
PETERSHOF