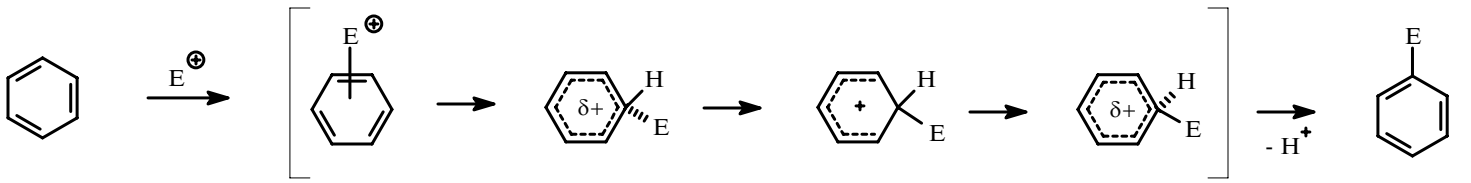
AROMATIČNE SUPSTITUCIJE

1) Elektrofilne

2) Nukleofilne

1) Elektrofilne aromatične supstitucije

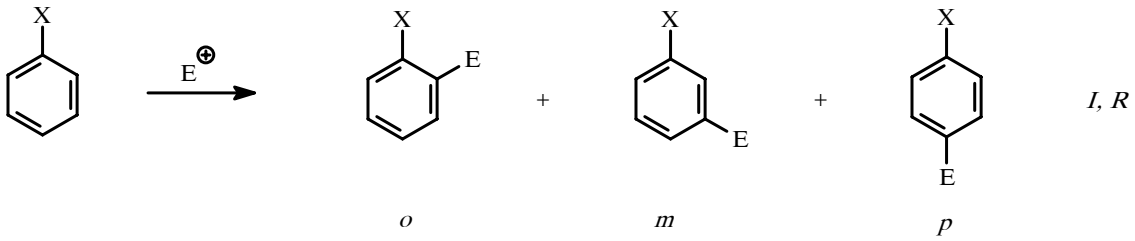


π-kompleks

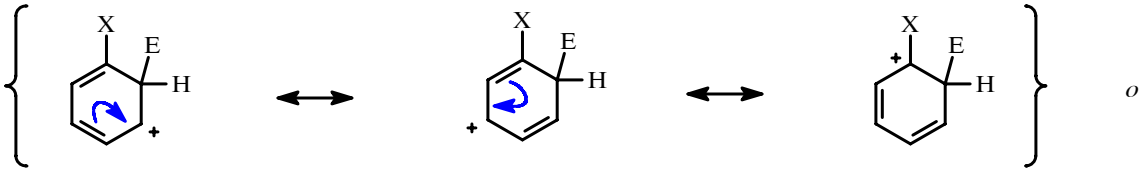
σ-kompleks (fenonijum jon, Wheland-ov intermedijer)

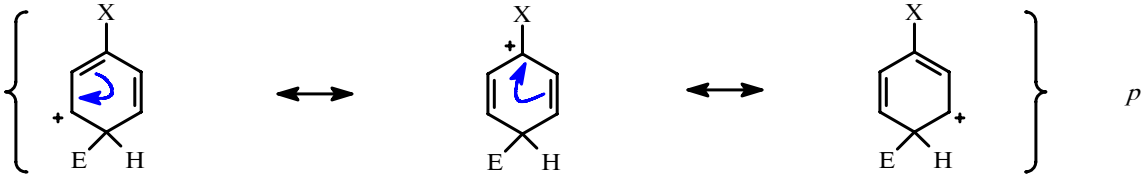
$E^{\oplus}$ = $R^{\oplus}$, $R\text{-}C^{\oplus}{=}O$, $X^{\oplus}$, $NO_2^{\oplus}$, $SO_3^{\oplus}$,...

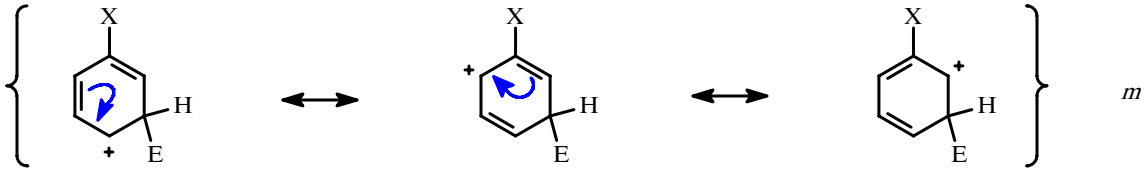
* Direkcioni efekti supstituenata

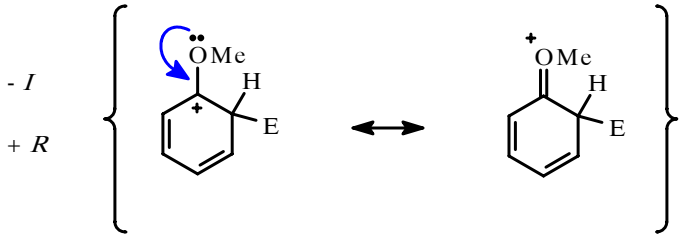


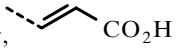
o *m* *p*

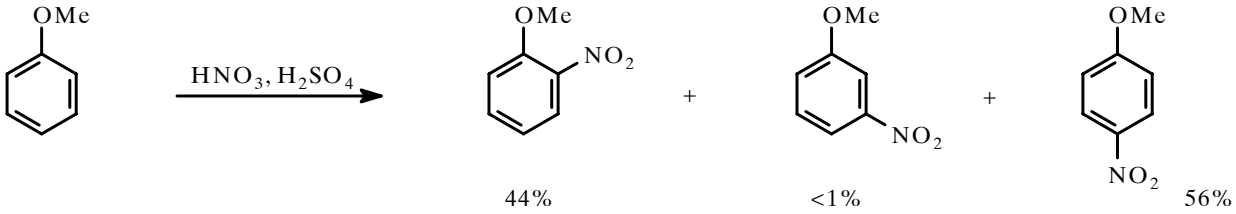




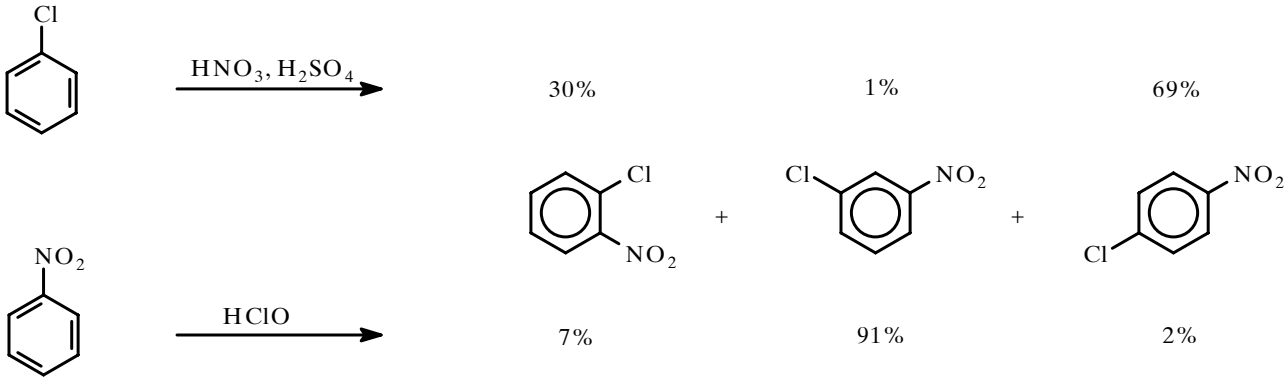


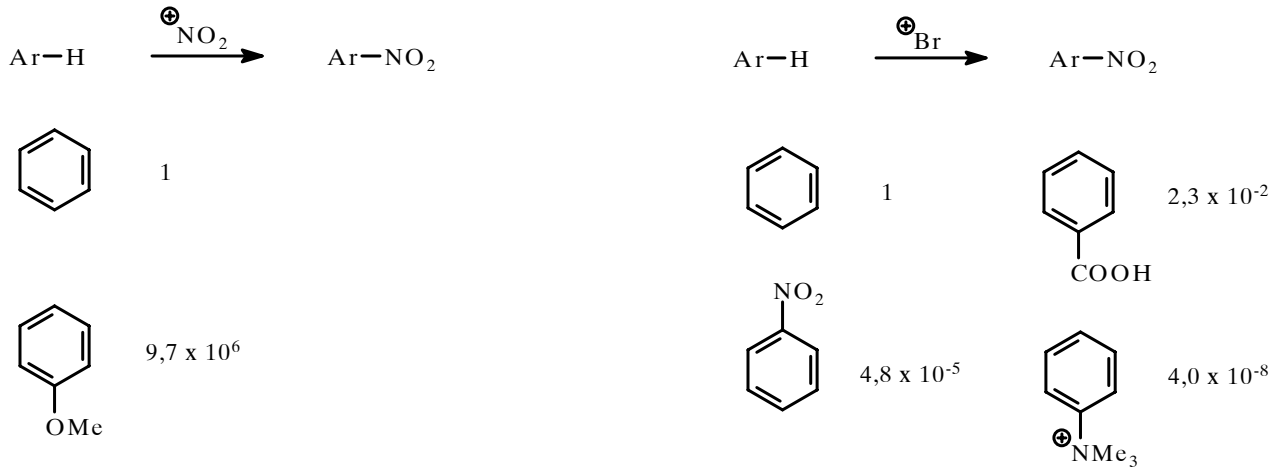


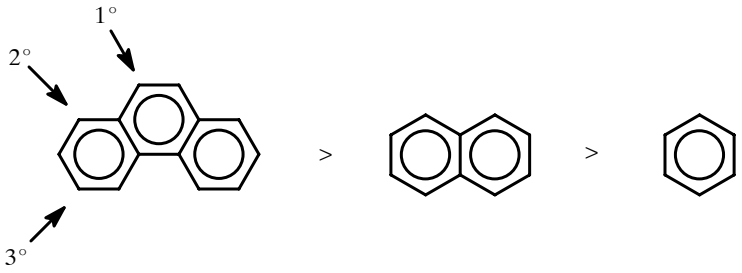
I	*R*	Supstituent	Uticaj na reaktivnost	Direkcioni efekat
+	+	alkil, O^-	aktivirajući	o, p
+	-	COO^-	aktivirajući	o, p
-	+	NR_2, $NHCO_2R$, Ph, OMe	aktivirajući	o, p
-	+	Cl, Br, 	dezaktivirajući	o, p
-	-	COR, CO_2R, SO_3H, CN, NO_2	dezaktivirajući	m



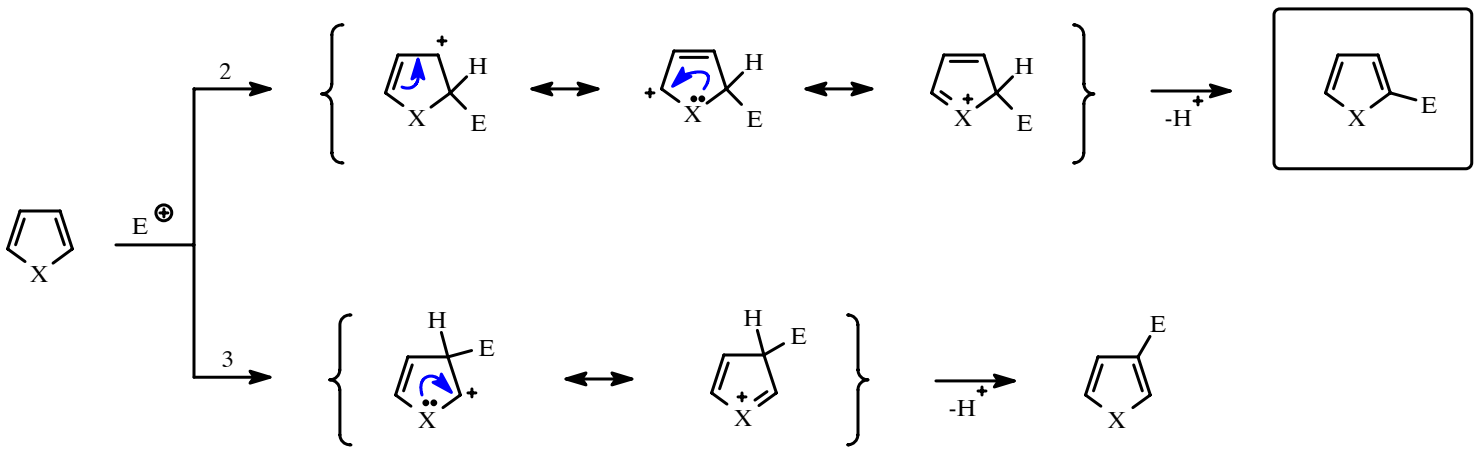
44% <1% 56%



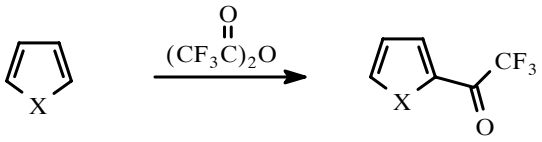

Ar–H
⊕NO2
Ar–NO2
1
9,7 x 10^6
OMe
Ar–H
⊕Br
Ar–NO2
1
2,3 x 10^-2
COOH
NO2
4,8 x 10^-5
4,0 x 10^-8
⊕NMe3


1°
2°
3°
>

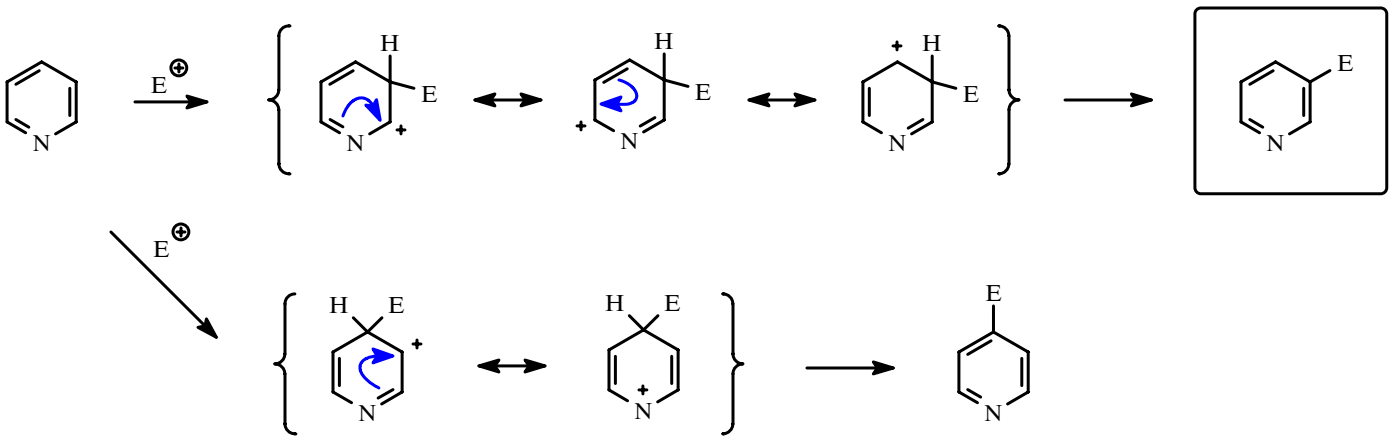

NH3
H
N
O

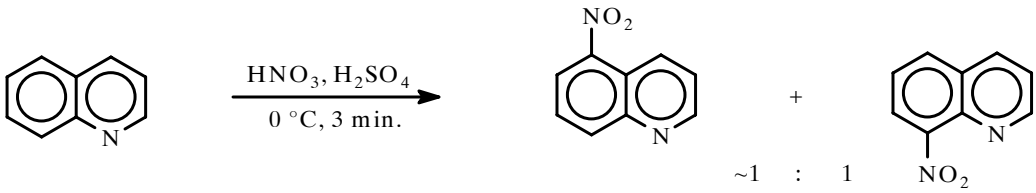

X
E⊕
2
3
H
E
-H+


N
H
O
S
N
>



X	K_{rel}
N	2×10^8
O	150
S	1





~1 : 1

* Katalizatori: H^+ i LA

$$HNO_3 + H_2SO_4 \longrightarrow \overset{+}{N}O_2 + H_2O + HSO_4^-$$

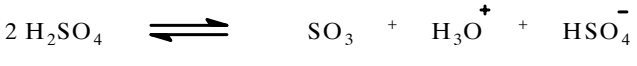
$$Cl_2 + FeCl_3 \longrightarrow Cl^+ \ ^-FeCl_4$$

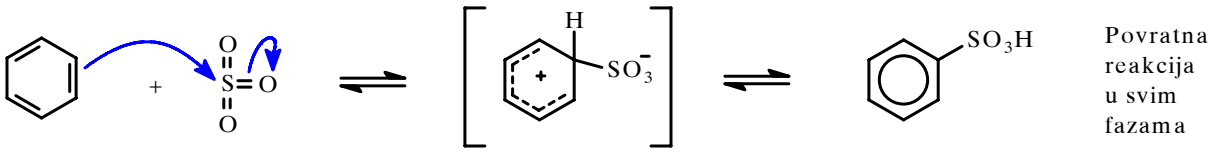
$$R\text{-}X + AlCl_3 \longrightarrow R^+ \ ^-AlCl_4$$

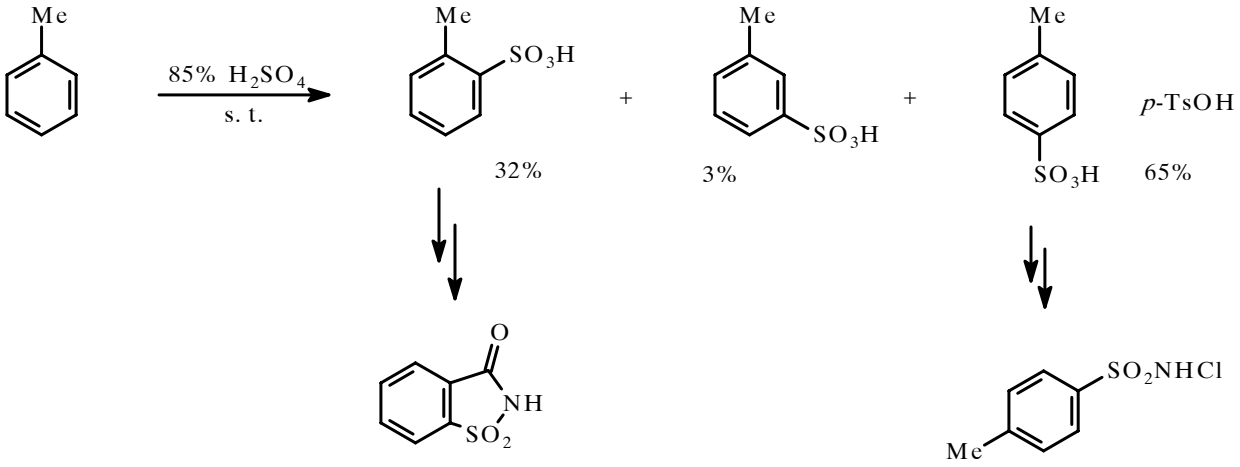
Sulfonovanje

Pušljiva H_2SO_4 > H_2SO_4 conc. > 80% H_2SO_4

Pyr• SO_3 : za osetljive sisteme

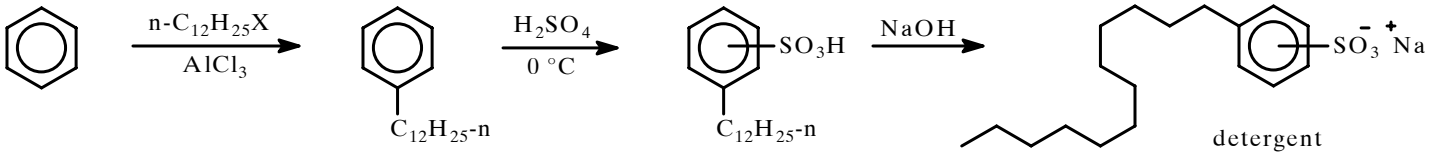


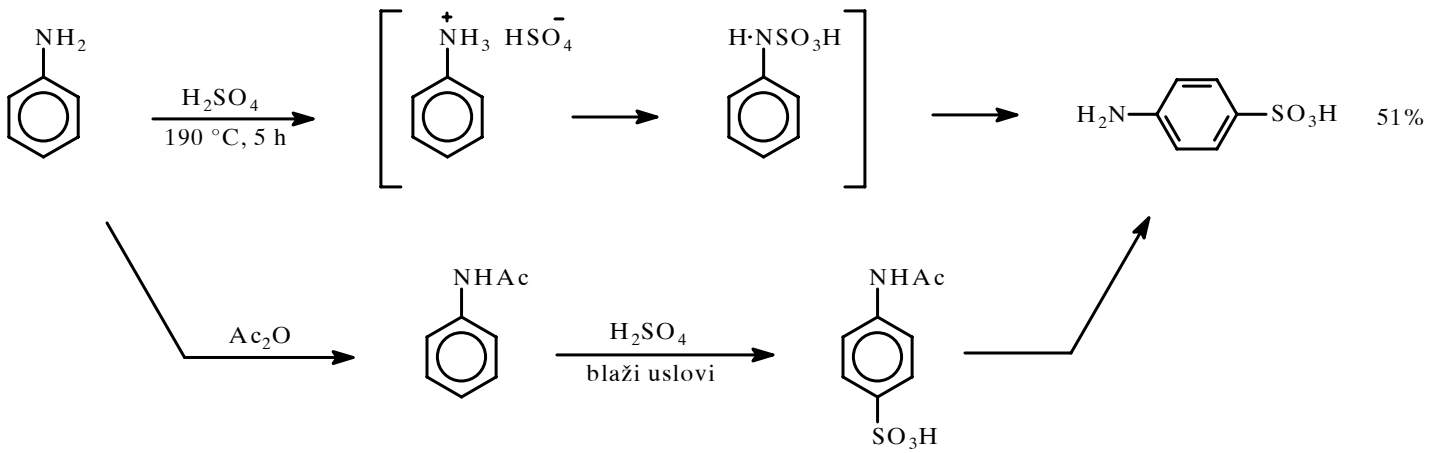


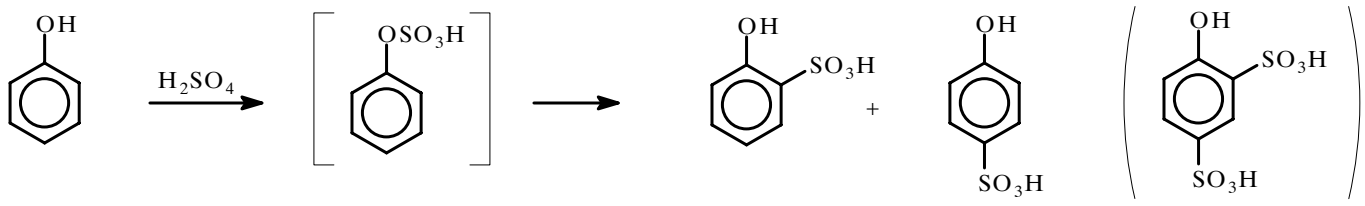


saharin

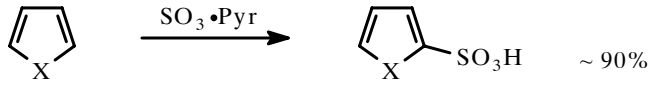
hloramin-T





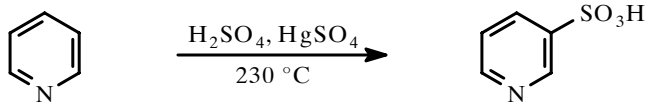


na 100 °C

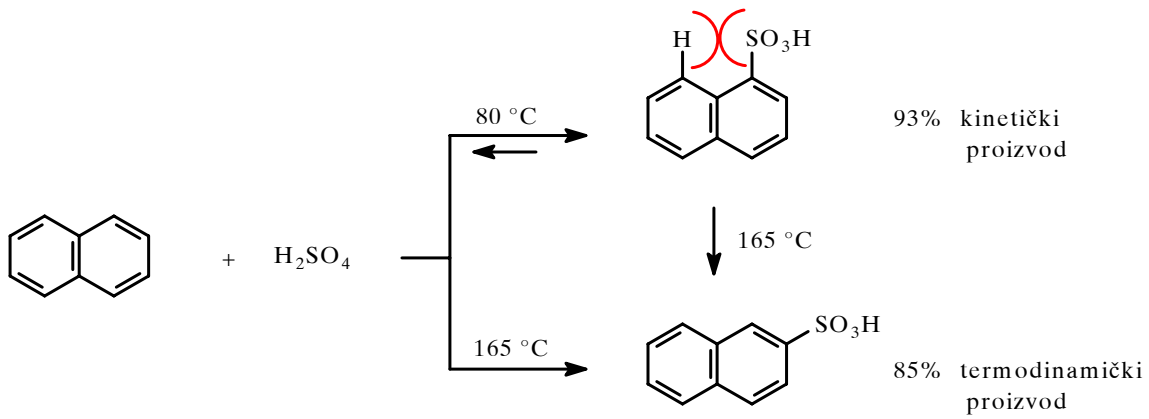


~ 90%

X = O, S, NH (sa H_2SO_4: otvaranje heterocikličnog prstena)



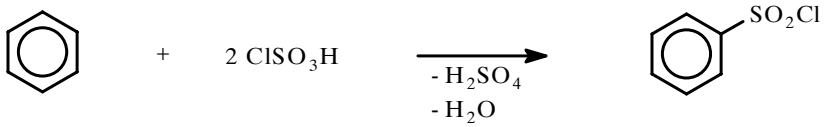
70%

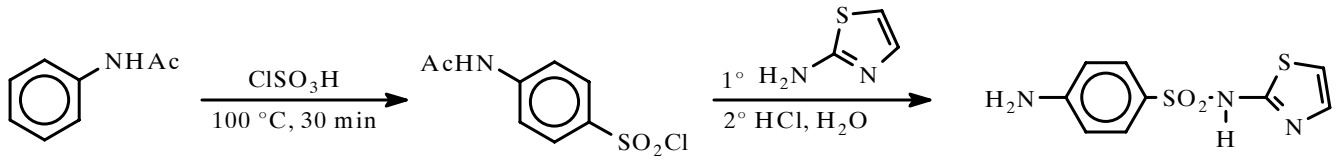


93% kinetički proizvod

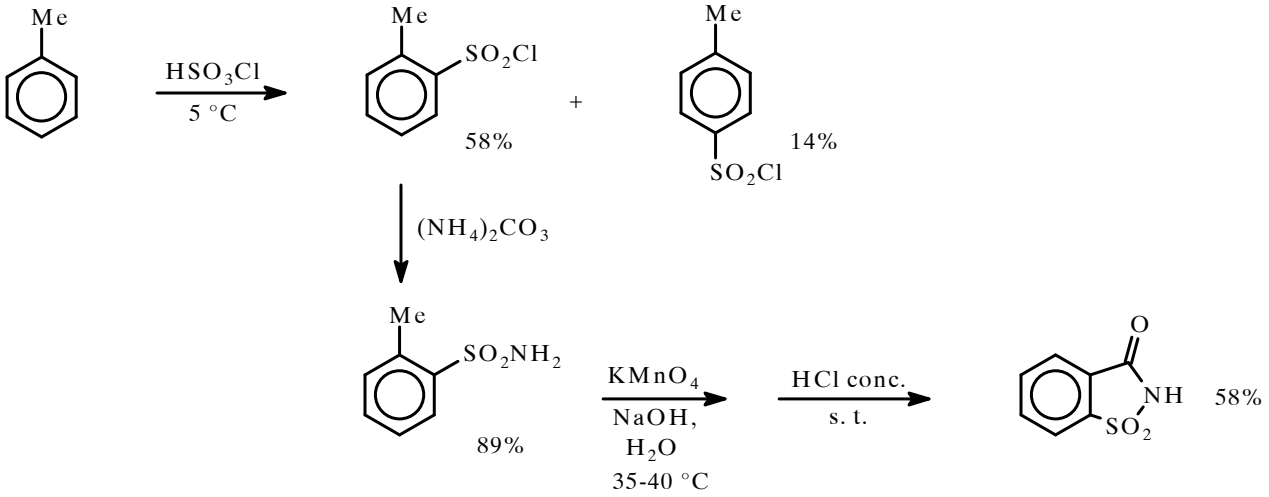
85% termodinamički proizvod

* $ClSO_3H$ Hlorsulfonska kiselina





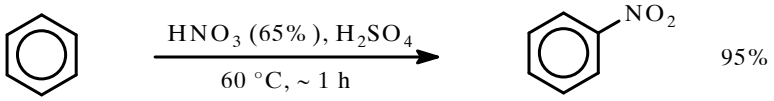
Sulfatiazol

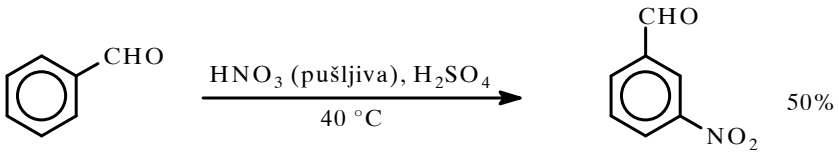


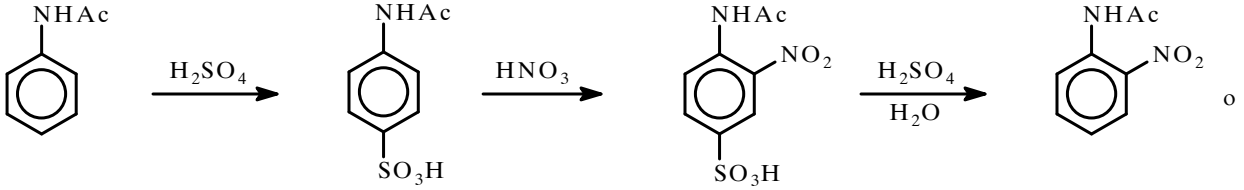
* Nitrovanje

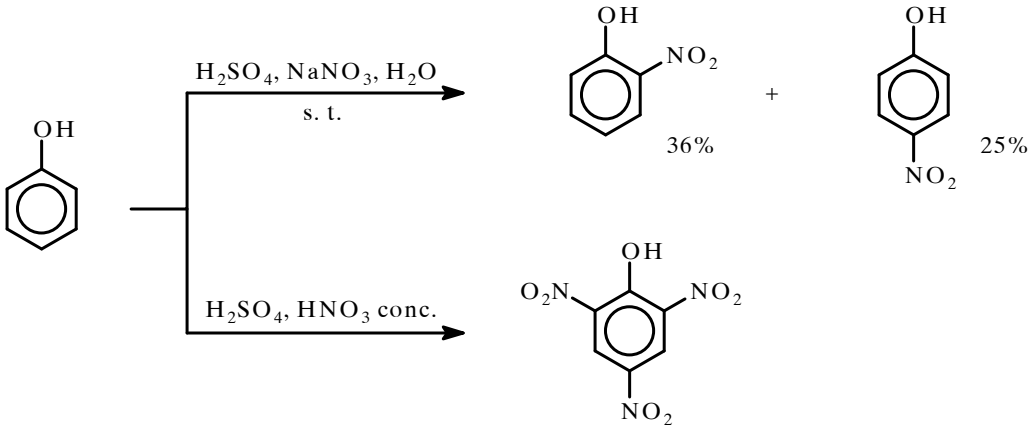
$$HNO_3\ (+AcOH, Ac_2O) < HNO_3 + H_2SO_4 < H_2SO_4 + KNO_3$$

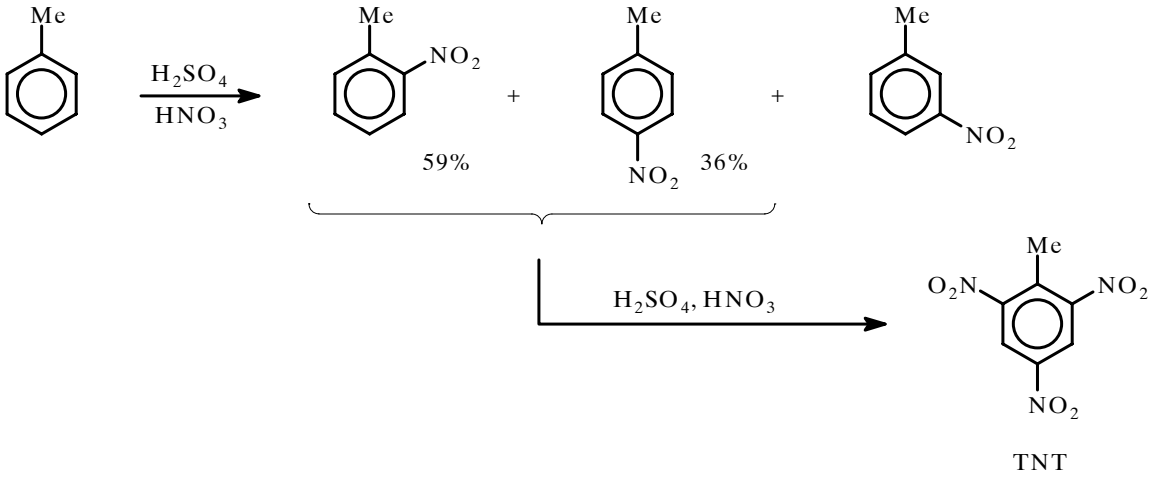
$$+ \quad NO_2 + H_2O + \bar{H}SO_4$$



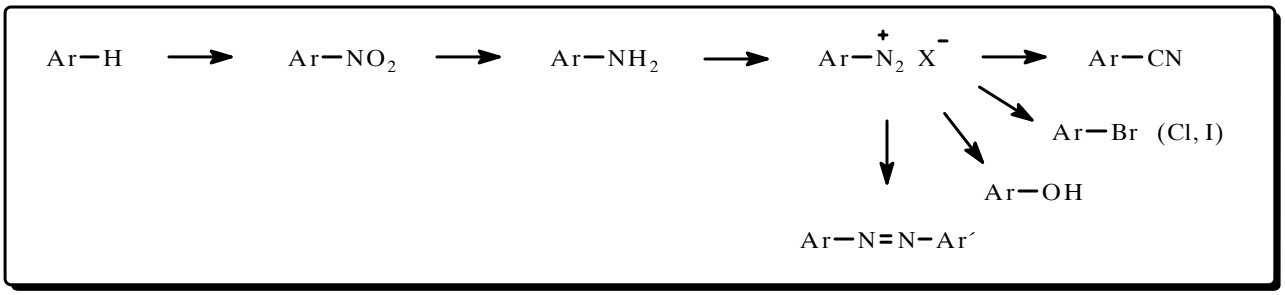


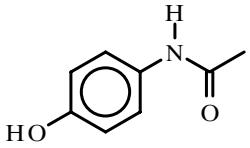




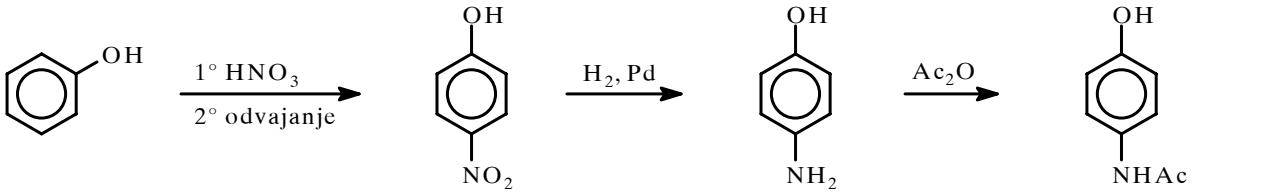


TNT

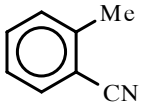


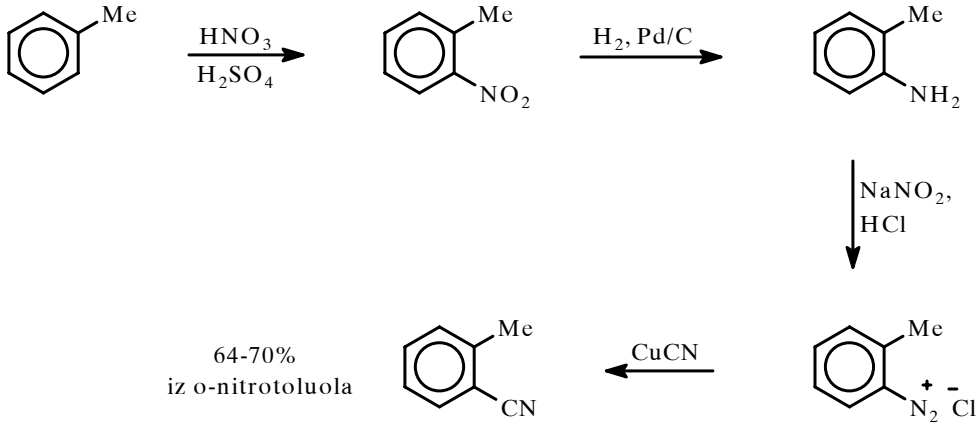


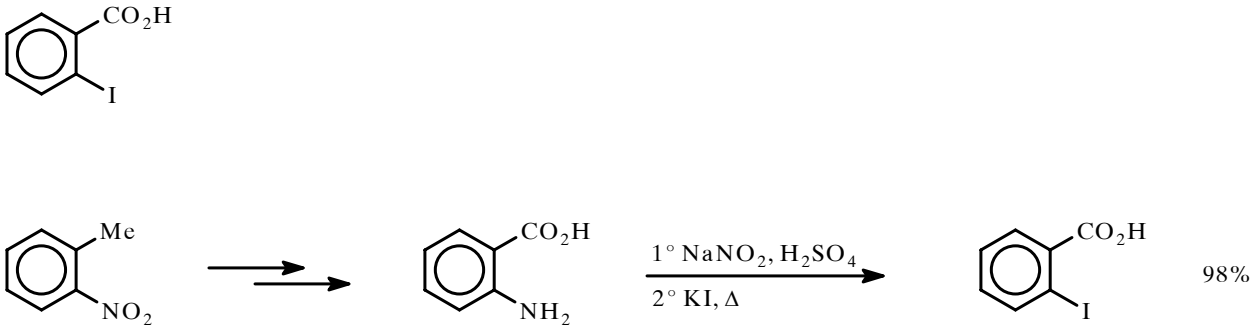
Paracetamol



79% (iz p-nitrofenola)

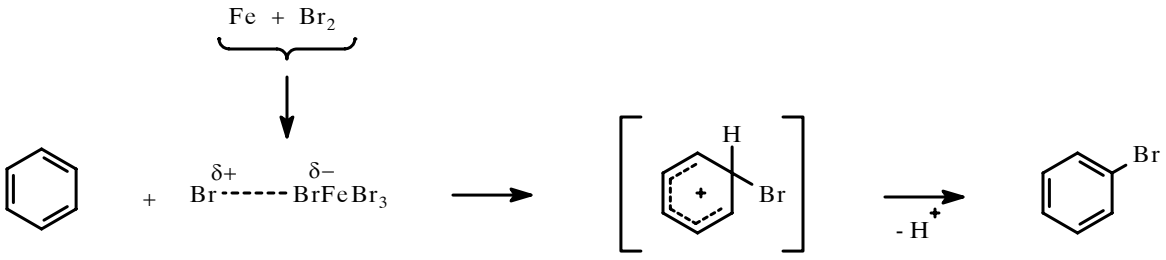


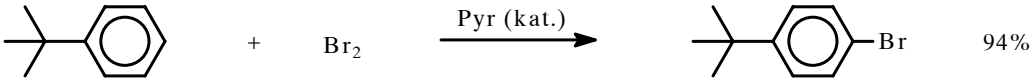


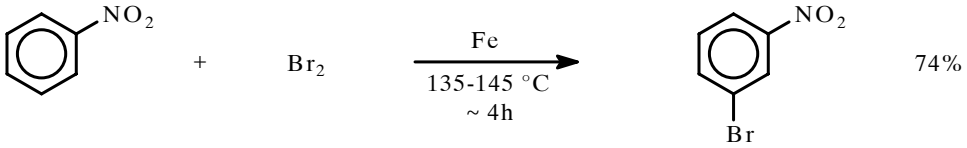


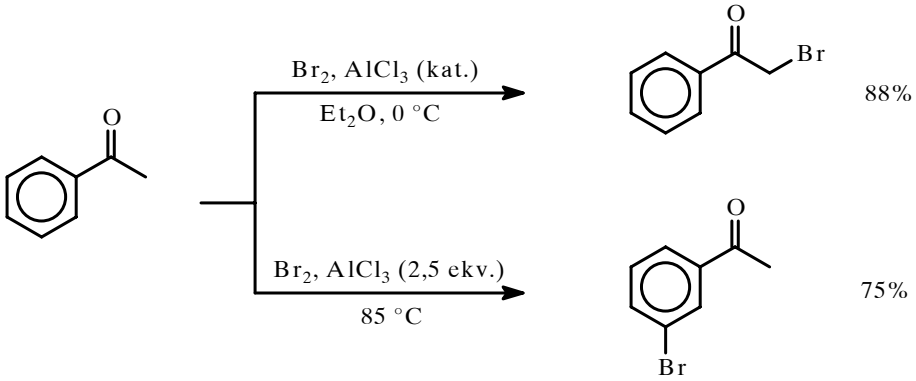
* Halogenovanje

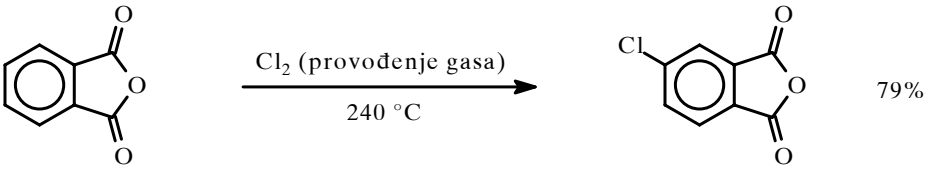
Reagensi: X_2/FeX_3, AlX_3, $ZnCl_2$; NBS; X_2/Ag_2SO_4; Py↑ HBr_3

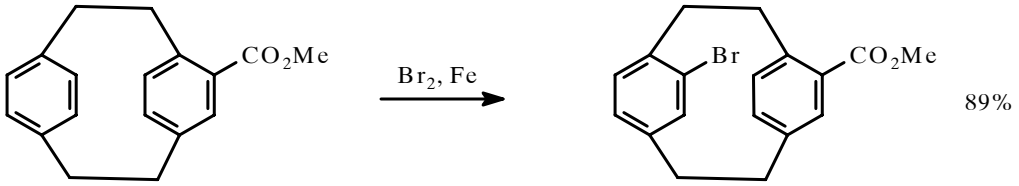


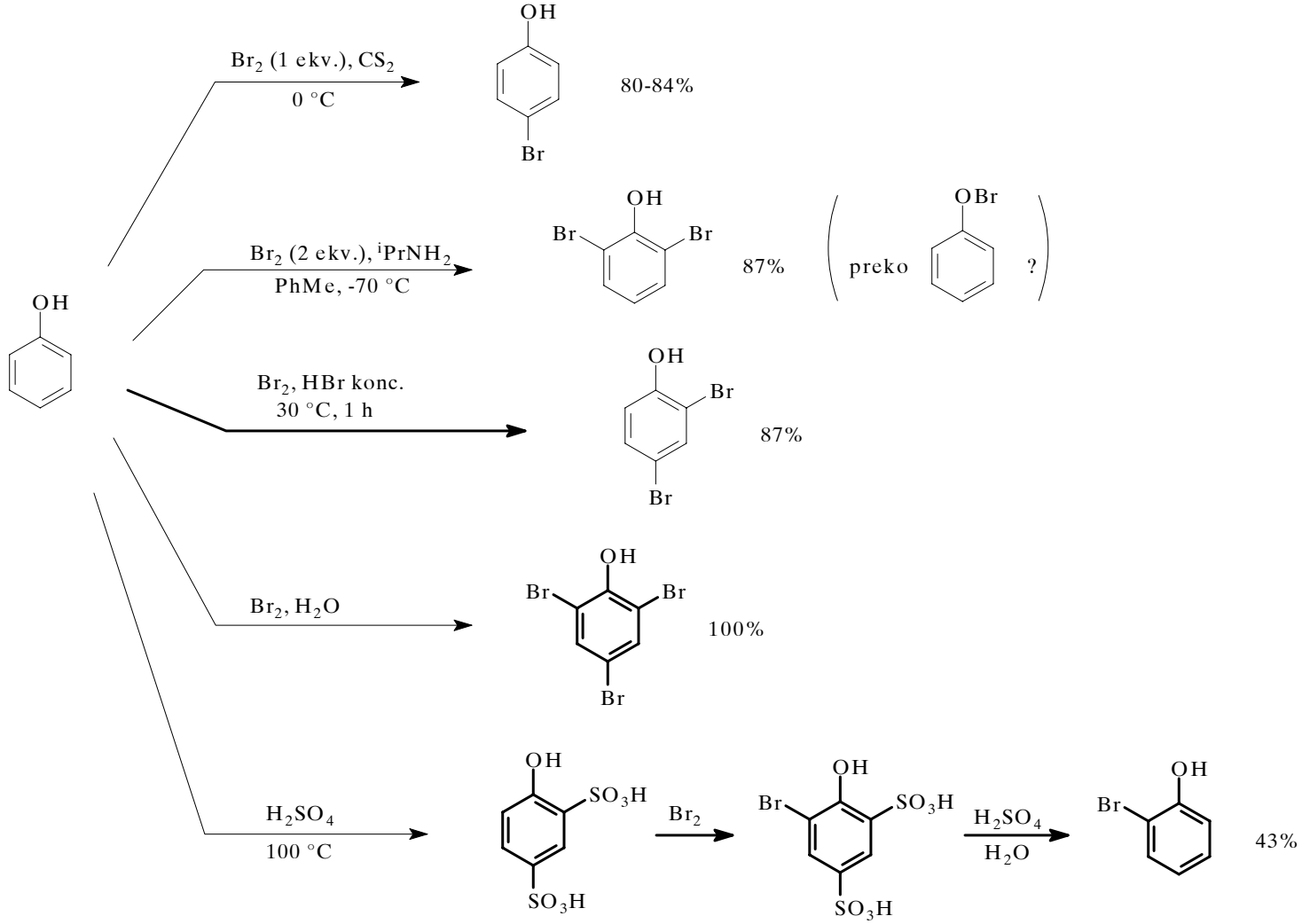

+
Br_2
Pyr (kat.)
Br
94%

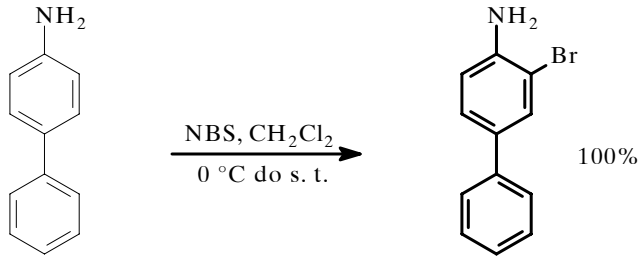

NO_2
+
Br_2
Fe
135-145 °C
~ 4h
NO_2
Br
74%

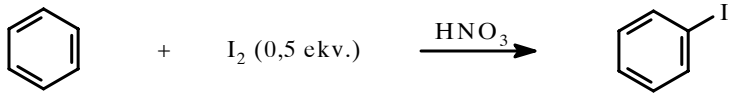

O
Br_2, $AlCl_3$ (kat.)
Et_2O, 0 °C
O
Br
88%
Br_2, $AlCl_3$ (2,5 ekv.)
85 °C
O
Br
75%

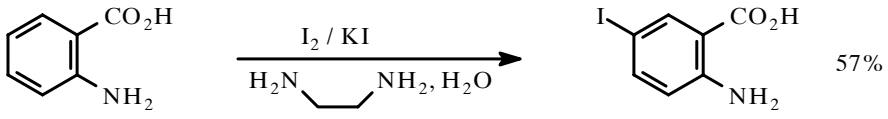

O
O
O
Cl_2 (provođenje gasa)
240 °C
Cl
O
O
O
79%

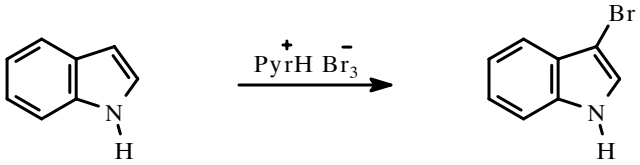

CO_2Me
Br_2, Fe
Br
CO_2Me
89%

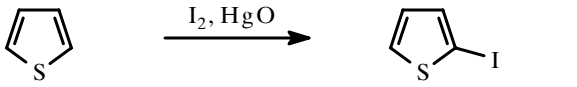

OH
Br2 (1 ekv.), CS2
0 °C
Br
80-84%
Br2 (2 ekv.), iPrNH2
PhMe, -70 °C
Br
Br
87%
preko
OBr
?
Br2, HBr konc.
30 °C, 1 h
87%
Br2, H2O
100%
H2SO4
100 °C
SO3H
Br2
H2SO4
H2O
43%


NH2
NBS, CH2Cl2
0 °C do s. t.
Br
100%

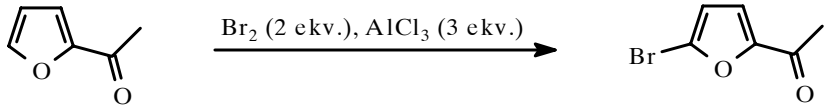

+
I2 (0,5 ekv.)
HNO3
I
87%


CO2H
NH2
I2 / KI
H2N
NH2, H2O
I
57%





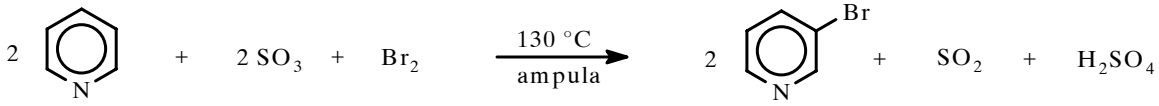
75%



62%

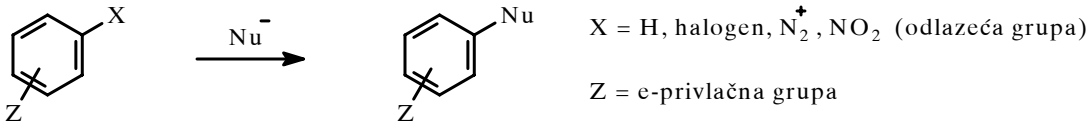
30-40%

nereaktivan



86%

2) Nukleofilne aromatične supstitucije



X = H, halogen, N_2^+, NO_2 (odlazeća grupa)

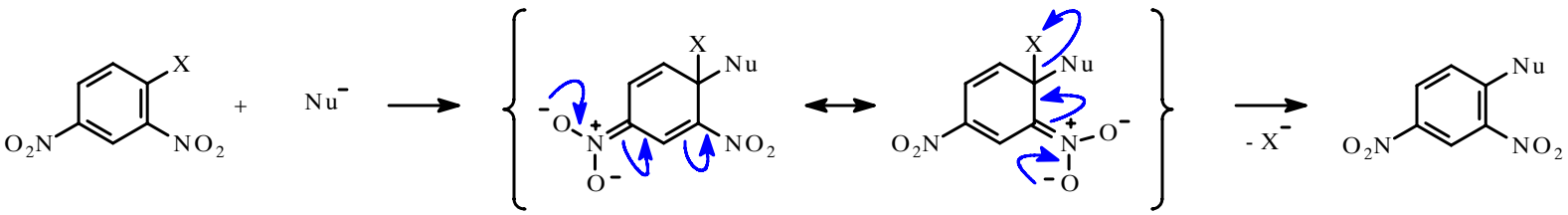
Z = e-privlačna grupa

* S_NAr

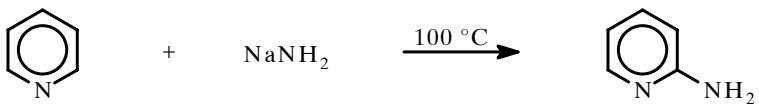
* S_R (preko aril-radikala)

* preko benzina (dehidrobenzena)

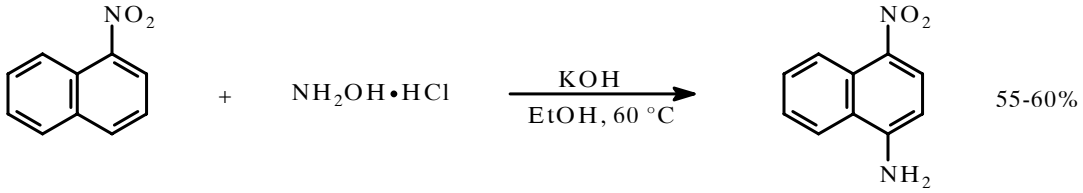
* S_NAr



H

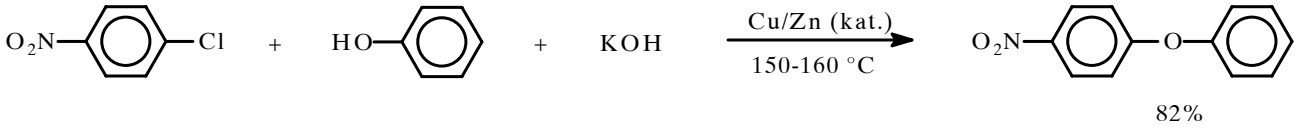


Chichibabin-ova reakcija

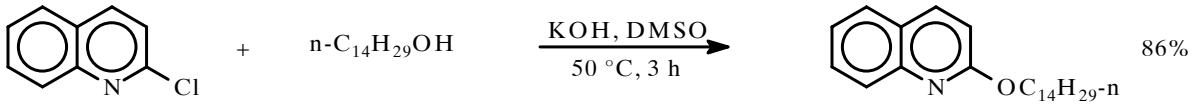


55-60%

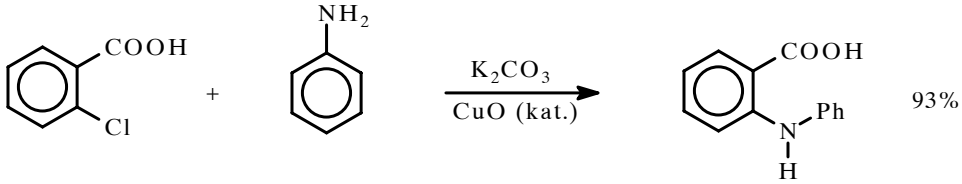
F, Cl, Br, I



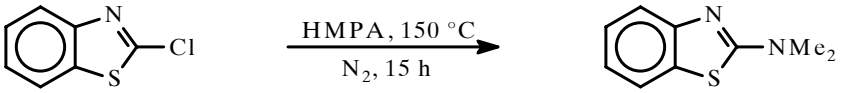
82%



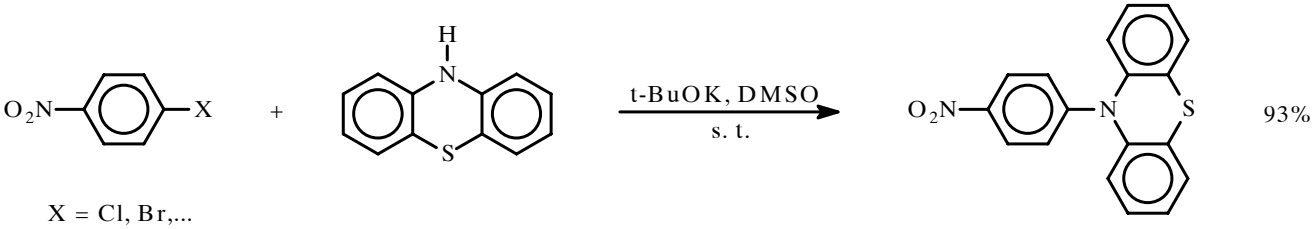
86%



93%

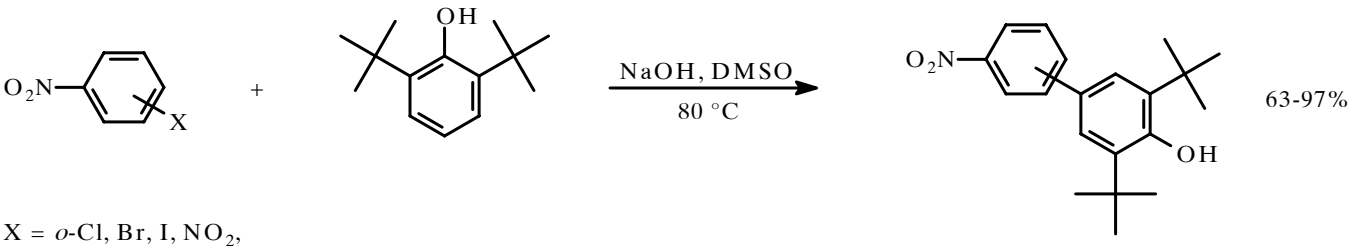


64%



93%

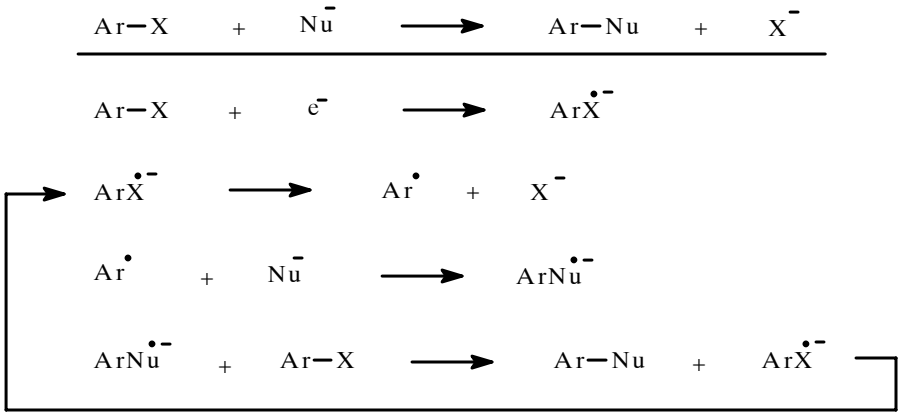
X = Cl, Br,...



63-97%

X = *o*-Cl, Br, I, NO_2,
p-NO_2, SO_2Ph

* $S_{RN}1$ pod dejstvom hv ili K/NH_3 liq.



X : I > Br > Cl > F; $(EtO)_2\overset{O}{\overset{\|}{P}}$-O-, $Me_3\overset{+}{N}$-

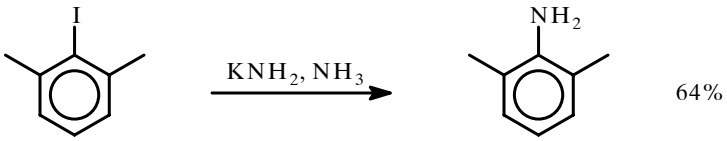
Rastvarač: NH_3 liq., DMSO, DMF; ponekad THF, DME

Supstituenti na Ar-jezgru: *o, m, p* - CN, C=O, MeO, NR_2 - pospešuju reakciju

$C\bar{O}O$, Ac, Bz - mogu biti prisutni

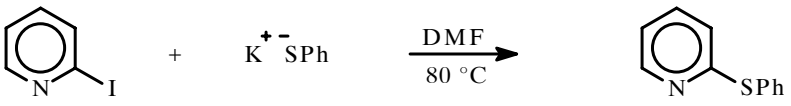
* Sa K / NH_3 česte su sporedne reakcije (npr. redukcija C=O grupe) $\Rightarrow$ bolje je NH_3 / *hv*

* Supstitucije heteroatomom



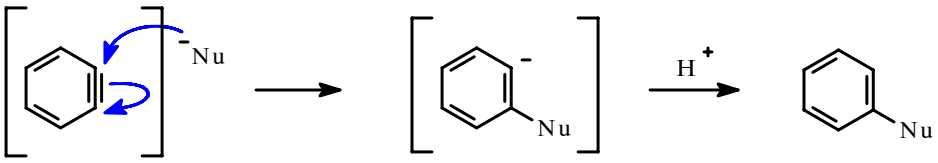
64%

ArO^-, $R\bar{O}$ ne reguju ($R\bar{O}$ + ArX $\xrightarrow{NH_3,\ hv}$ ✗ ArOR)

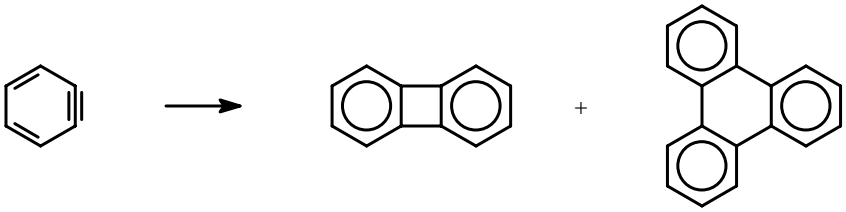


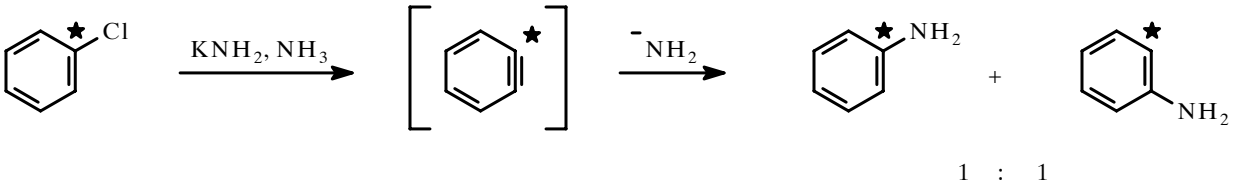
58%

* Supstitucije preko benzina (dehidrobenzena)

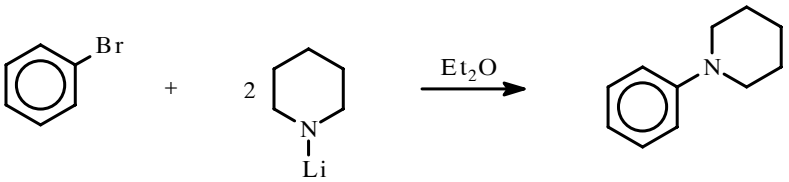


* Preparativno dobijanje benzina: *in situ* (vidi DA)
* Sporedne reakcije: cikloadicije, dimerizacija

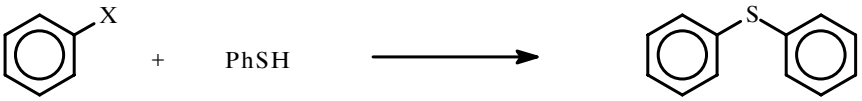




1 : 1

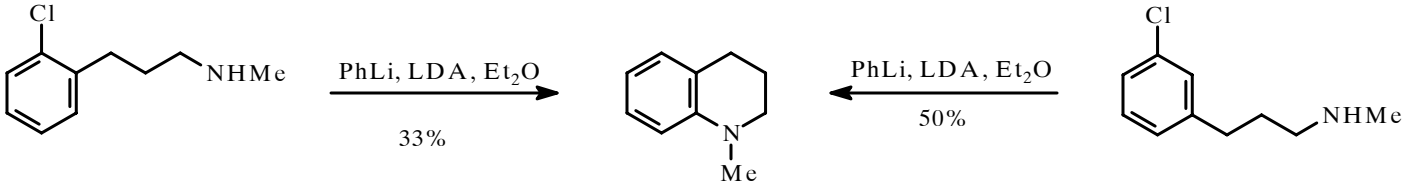


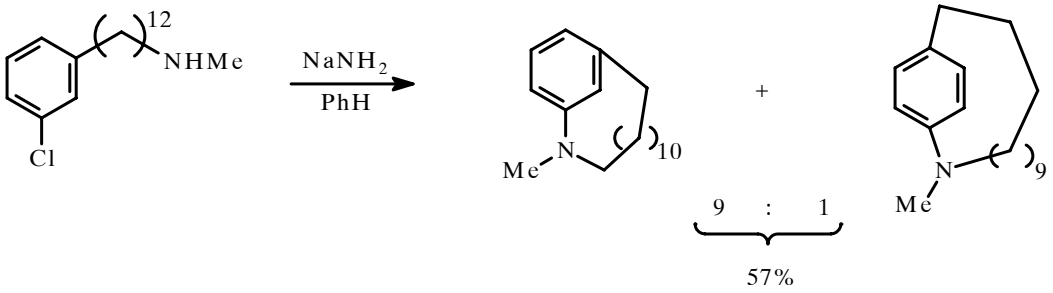
94%



KNH_2 / NH_3 42%

KO-t-Bu / DMSO >90%





9 : 1

57%