

Sulfinati i njihova primjena u organskoj sintezi

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Mia Bušljeta, Kemijski seminar I

24. travanj 2024.

💡 Organosumporovi spojevi

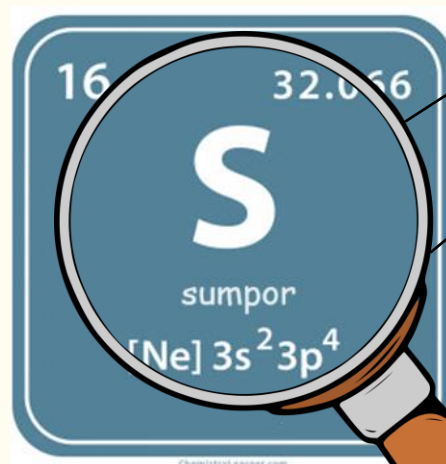
❓ Živi organizmi

🔪 Funkcionalni materijali

💊 Lijekovi

🍀 Agrokemikalije

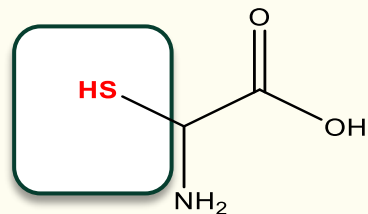
The periodic table shows elements from Hydrogen (H) to Oganesson (Og). A magnifying glass is positioned over the sulfur (S) element, which is located in the 16th group and 3rd period. The sulfur element box is highlighted with a magnifying glass effect.



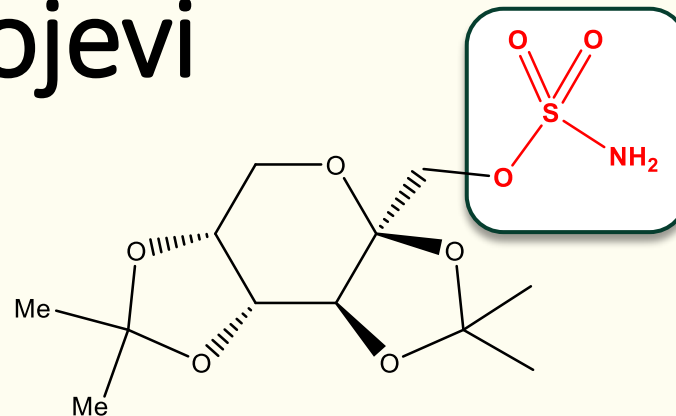
Legend for the periodic table color-coding:

- Alkali Metal
- Alkaline Earth
- Transition Metal
- Basic Metal
- Semimetal
- Nonmetal
- Halogen
- Noble Gas
- Lanthanide
- Actinide

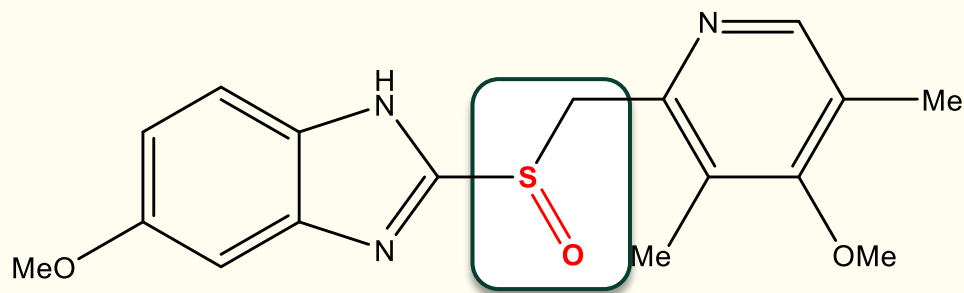
💡 Organosumporovi spojevi



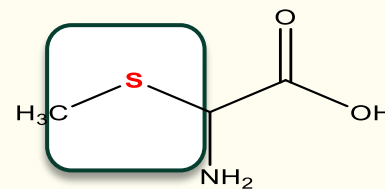
tiol
(cistein)



sulfamat
(topiramat, inhibitor ugljične
anhidraze)



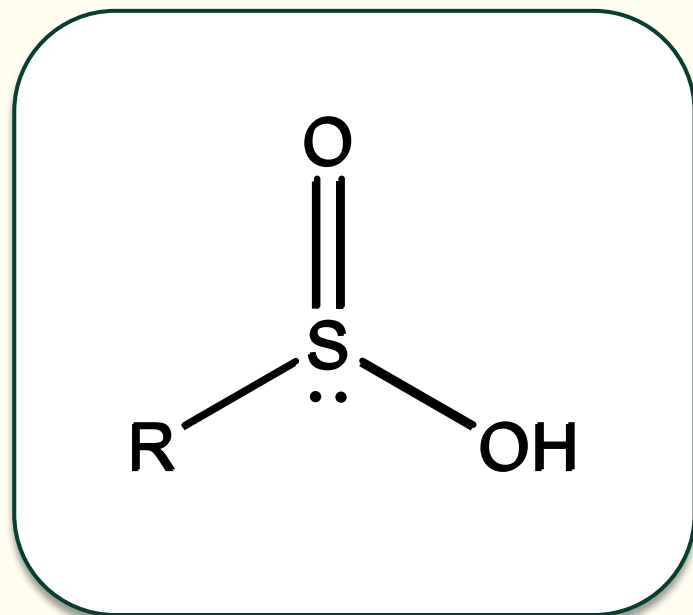
sulfoksid
(omeprazol – inhibitor protonske pumpe)



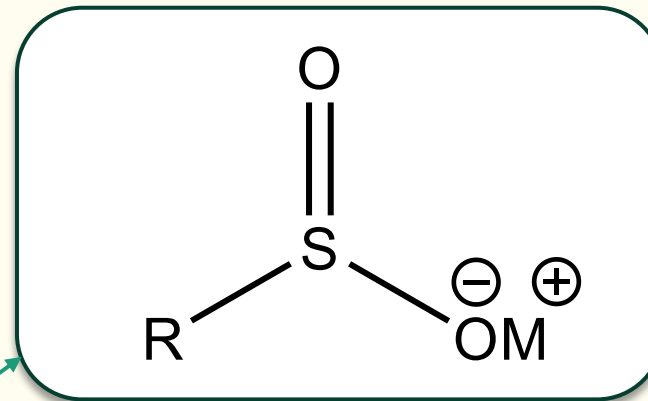
tioeter
(metionin)

Slika 1. Strukture biološki važnih organosumporovih spojeva

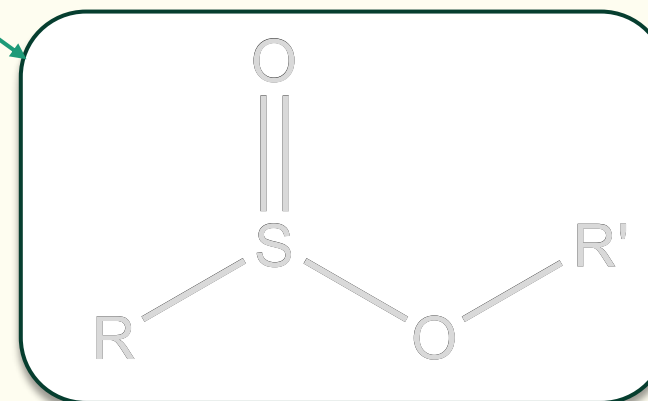
💡 Sulfinati



sulfinska kiselina



sol sulfinske kiseline



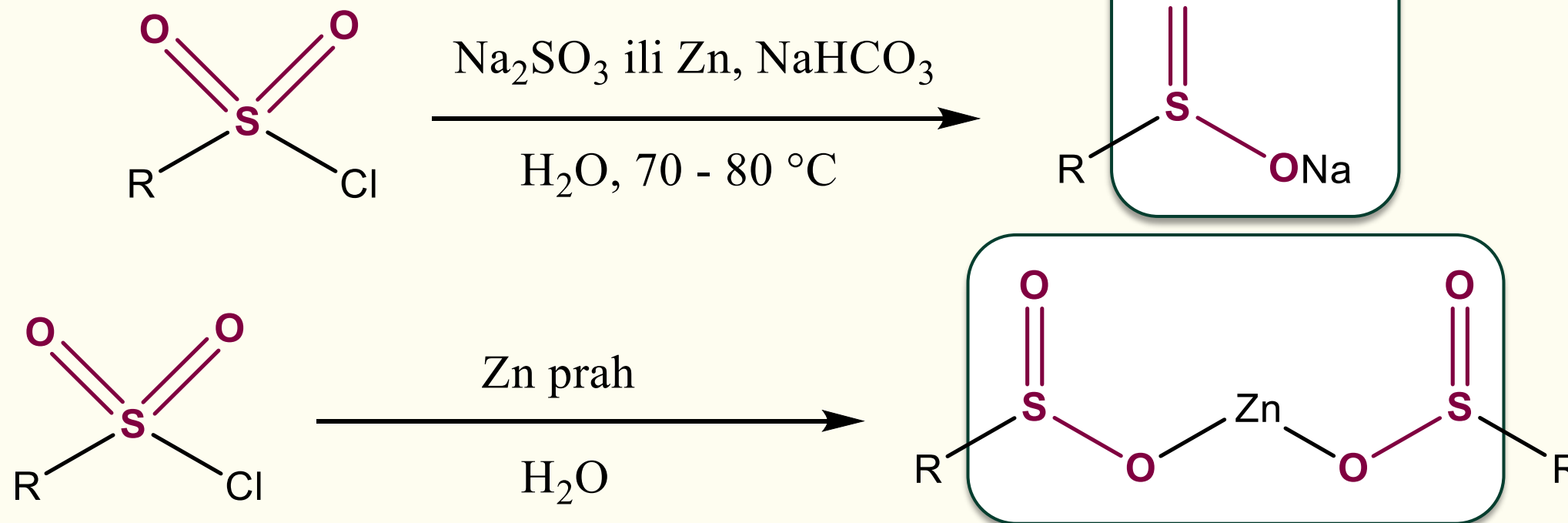
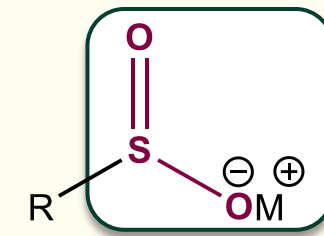
ester sulfinske kiseline

Slika 2. Strukture sulfinske kiseline i sulfinata



Sulfinatne soli

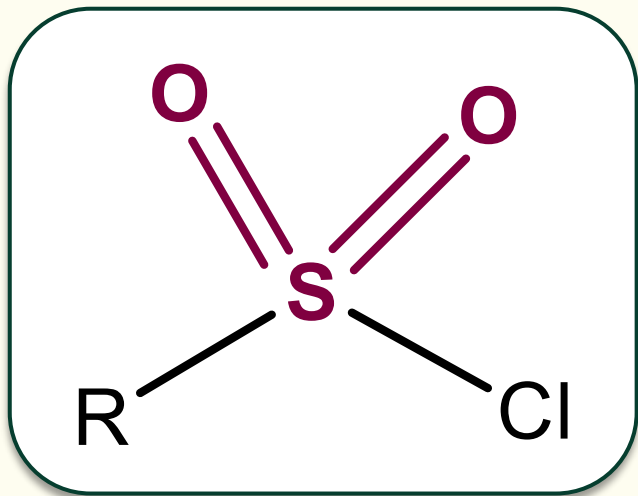
- ✓ Stabilne, netoksične i jeftine
- ✓ Natrijeve i cinkove najčešće korištene



Slika 3. Reakcije dobivanja sulfinatnih soli

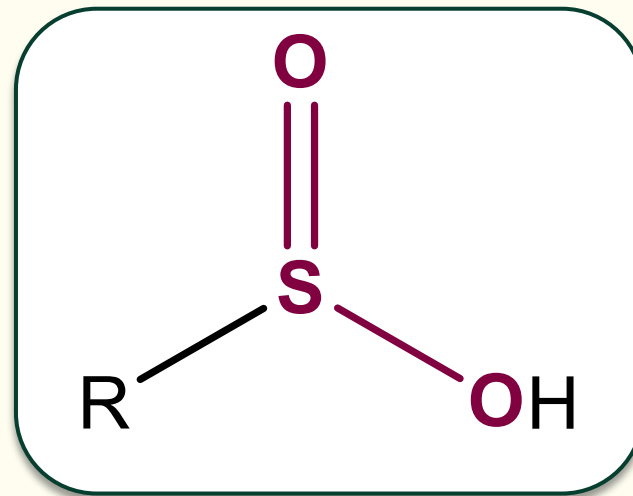


Sulfinske kiselina i sulfonil-kloridi



Sulfonil-klorid

- ✓ Važni prekursori za dobivanje drugih derivata
- ✓ Jako reaktivni i higroskopi

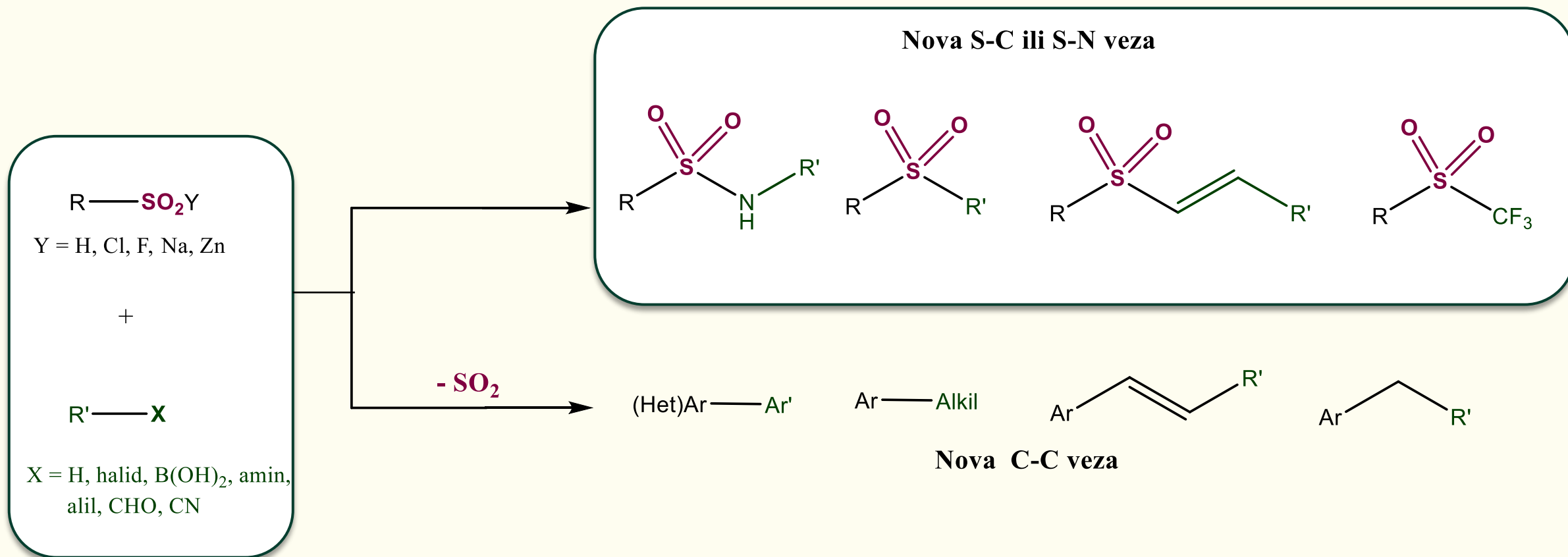


Sulfinska kiselina

- ✓ Sklone disproporcioniranju na tiosulfonate i sulfonske kiseline
- ✓ Aromatske relativno stabilne

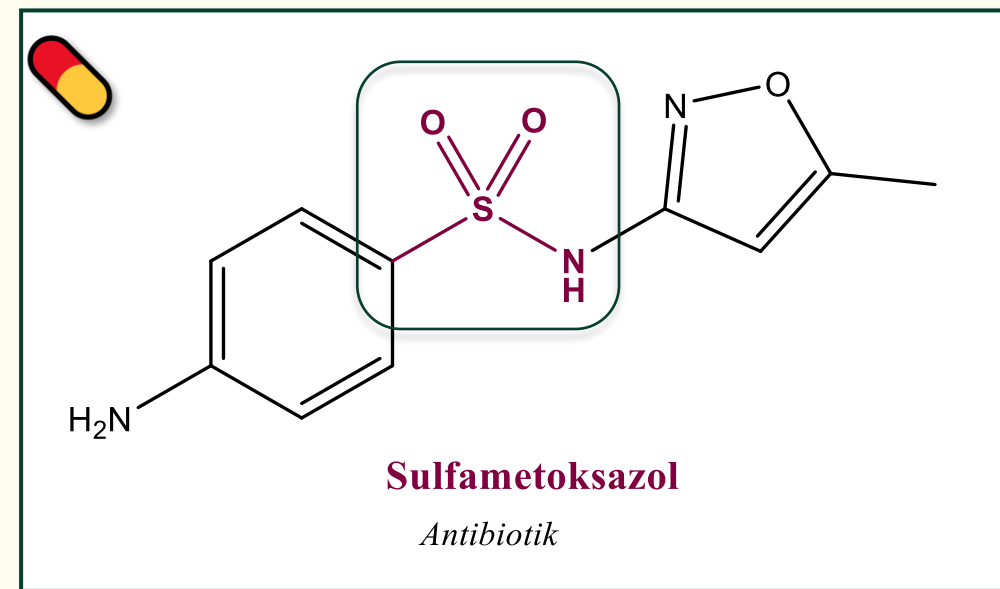
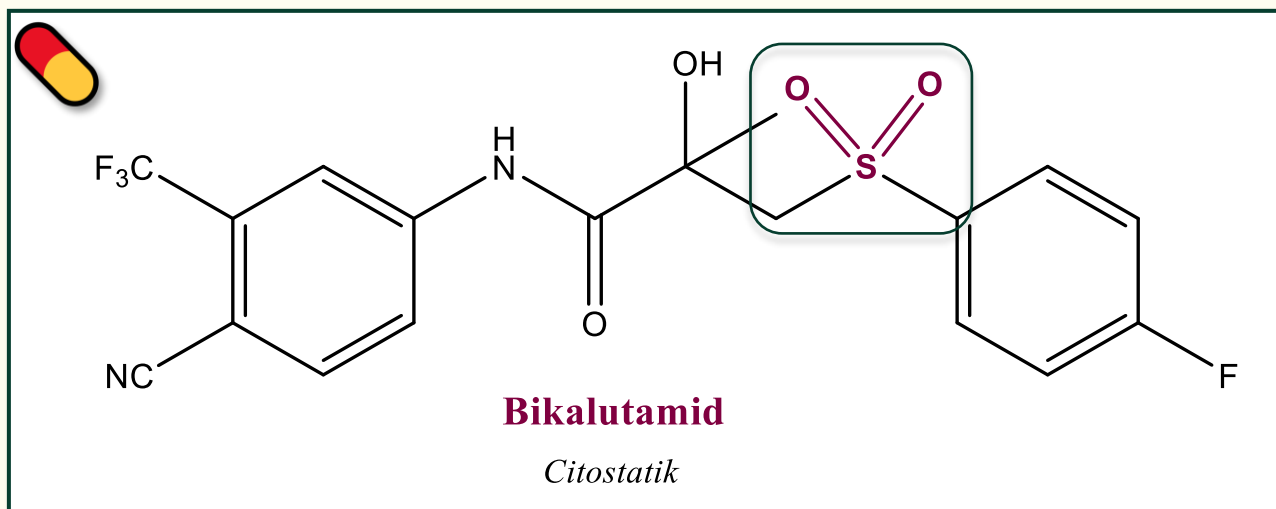
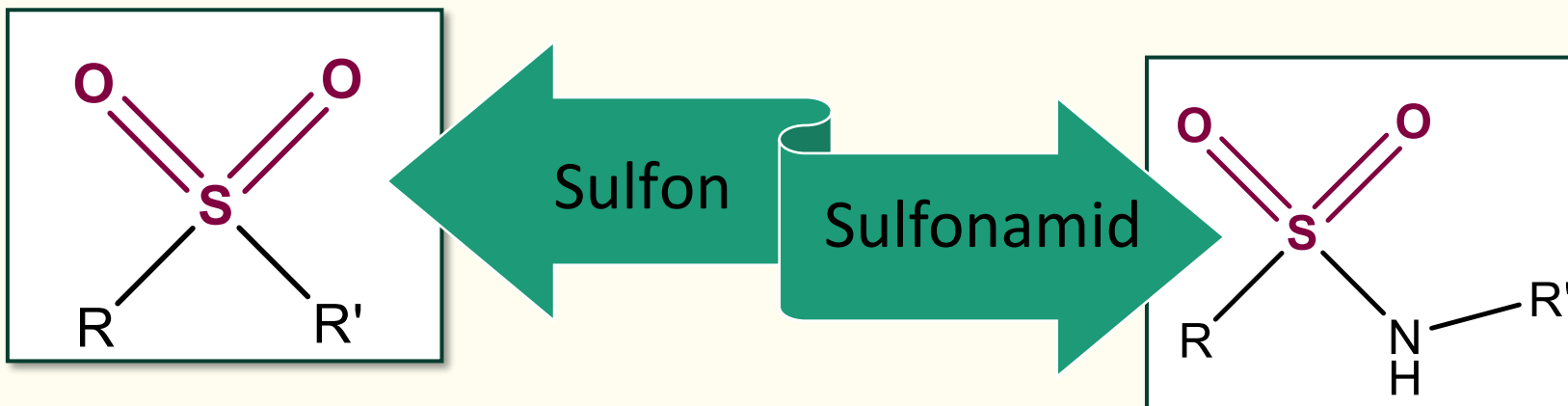
Slika 4. Strukture sulfonil-klorida i sulfinske kiseline

Reakcije sulfinata



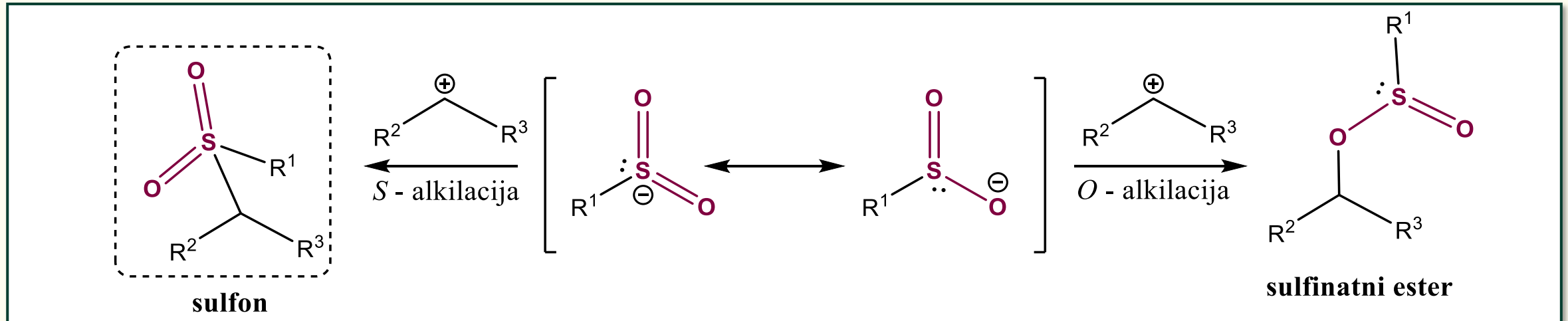
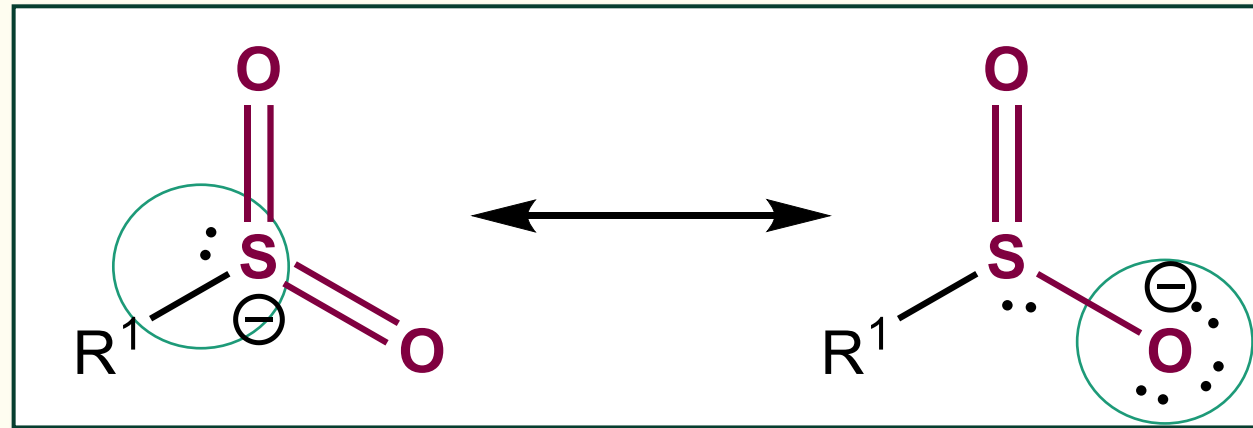
Slika 5. Opći prikaz reakcija sulfinata

💡 Sulfonska i sulfonamidna funkcijska skupina



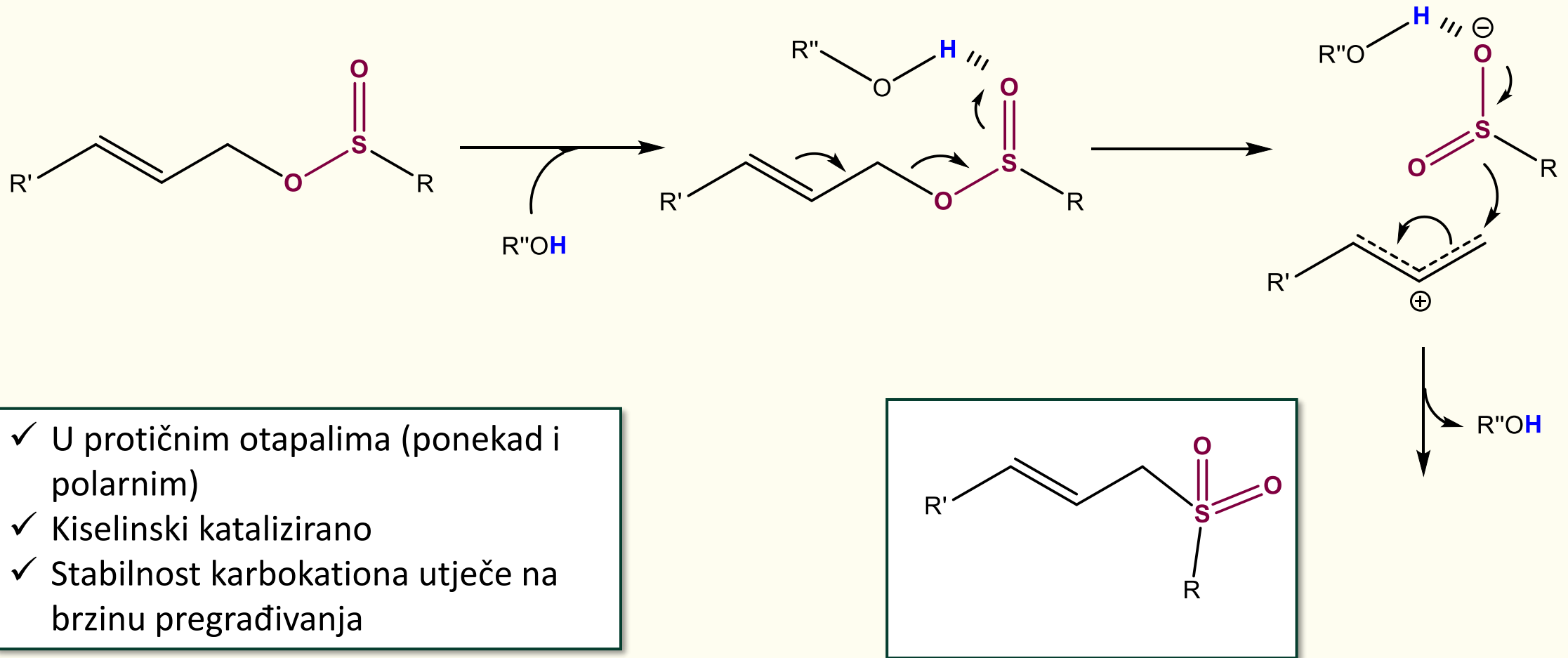
Slika 6. Strukture sulfonske i sulfonamidne skupine (gore) i njihovih biološki aktivnih spojeva (dolje)

💡 Ambidentno ponašanje sulfinatnog aniona



Slika 7. Abidentno ponašanje sulfinatnog aniona

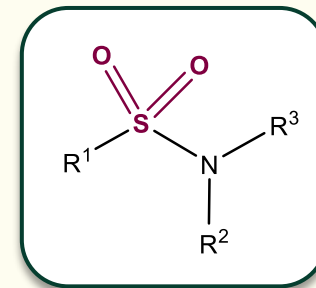
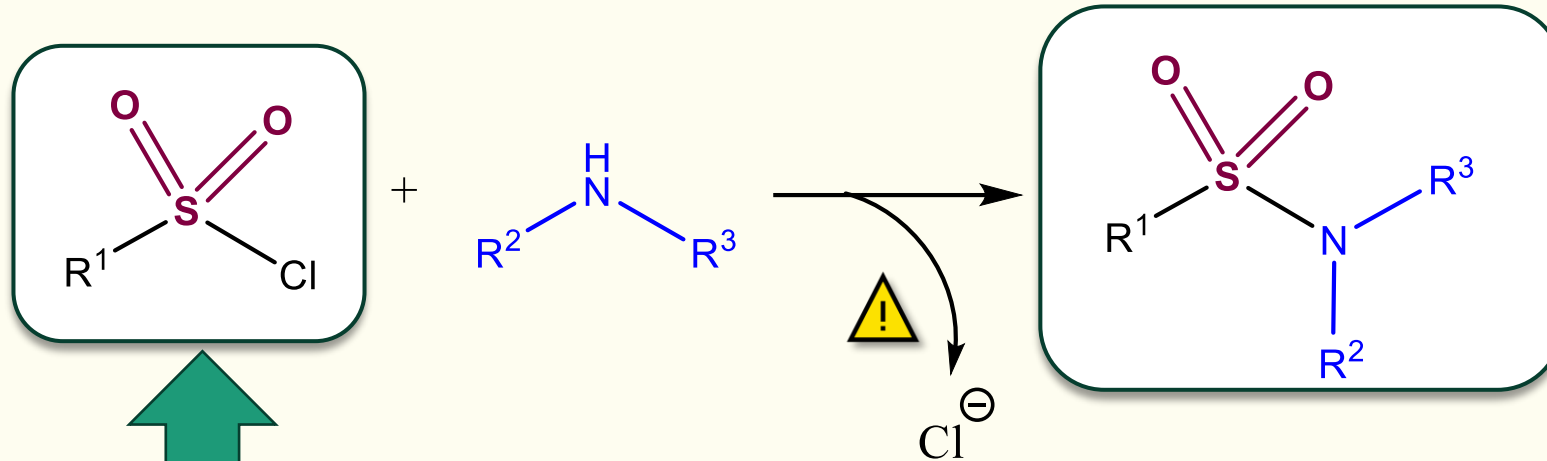
💡 Pregrađivanje sulfinata u sulfon



Slika 8. Mehanizam pregradnje sulfinatnog estera u sulfon



Sinteza sulfonamidne podjedinice

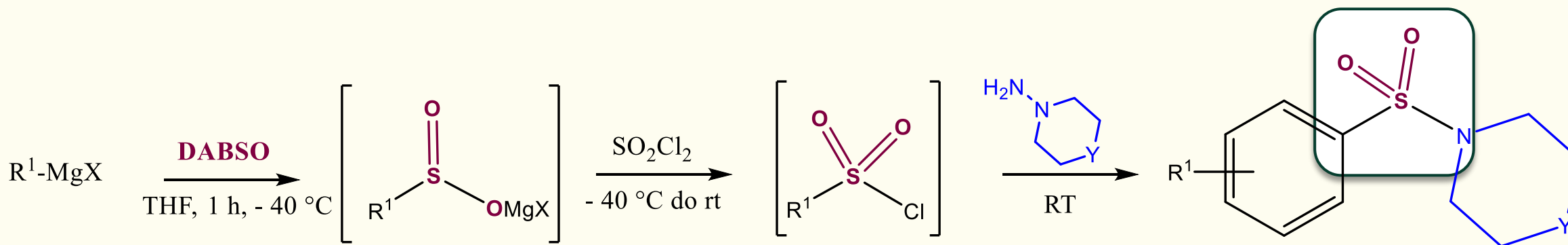
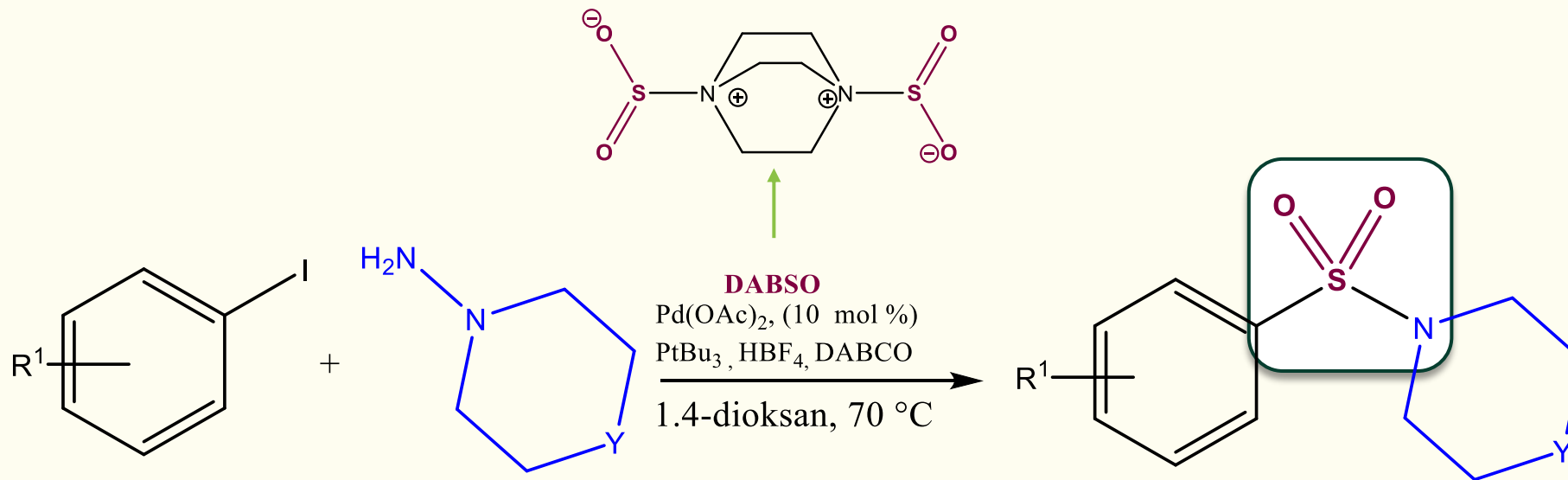
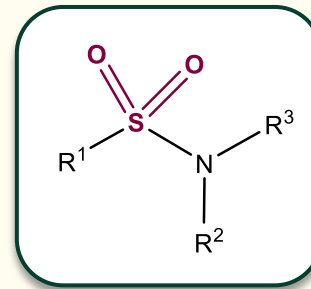


⚠ *in situ* generiranje
oksidacija tiola

Slika 9. Način priprave sulfonamidne funkcijske skupine



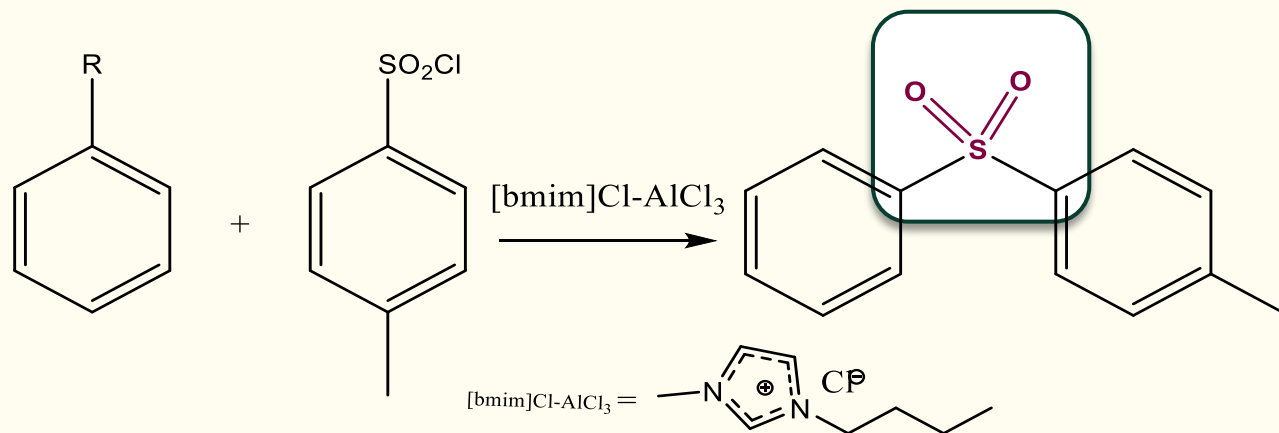
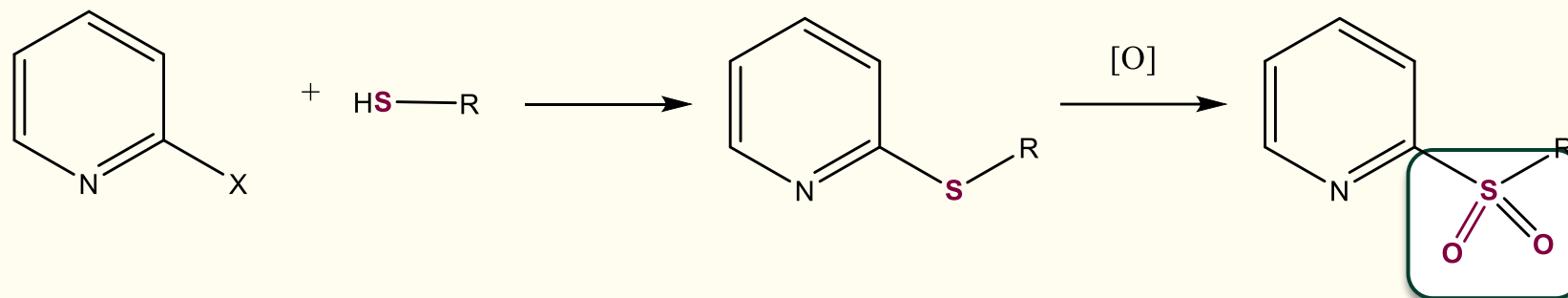
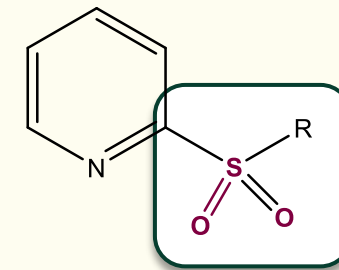
Sinteza sulfonamidne podjedinice



Slika 10. Struktura DABSO-a (gore) i načini priprave sulfinamidne funkcijske skupine (dolje)



Uvođenje sulfonske skupine na (hetero)aromatske spojeve

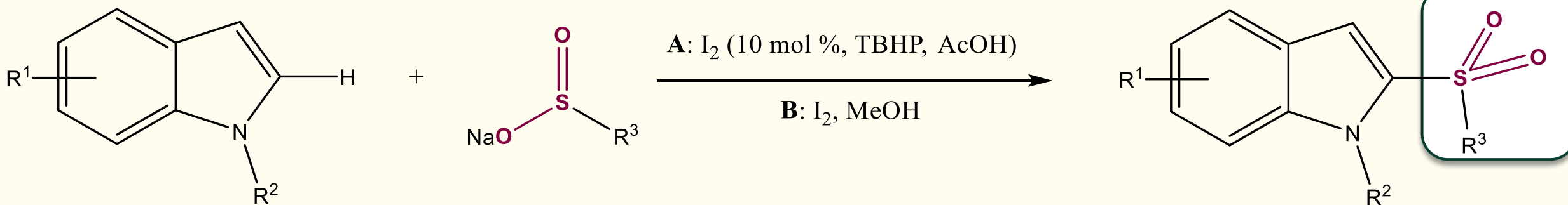
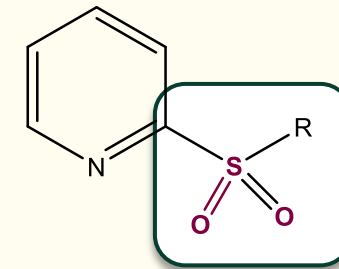


- x Neugodan miris tiola
- x Žestoki reakcijski uvjeti
- x Netolerancija prema drugim funkcijskim skupinama

Slika 11. Uvođenje sulfonske skupine na aromatski prsten



Uvođenje sulfonske skupine na (hetero)aromatske spojeve



$R^1 = \text{H, Me, Br, Cl}$

$R^2 = \text{H, Me}$

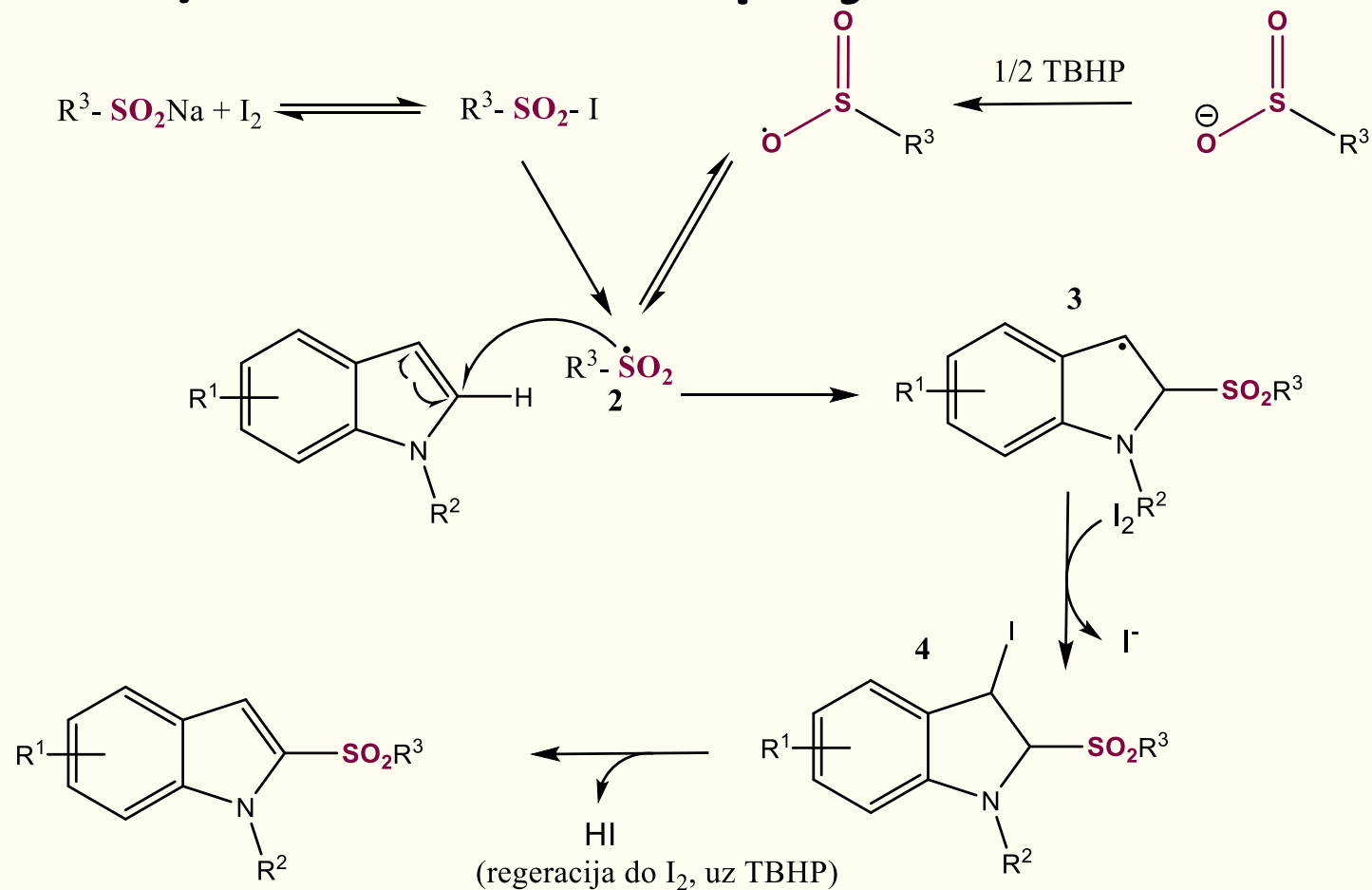
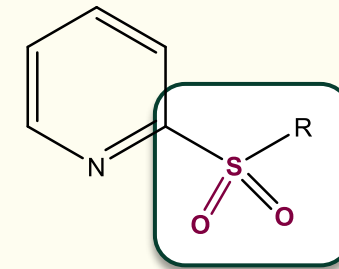
$R^3 = \text{Aril, Alkil}$

- ✓ Nije potreba ranija funkcionalizacija prstena
- ✓ Regioselektivnost

Slika 12. Način priprave sulfonske skupine uz pomoć joda i sulfinatne soli



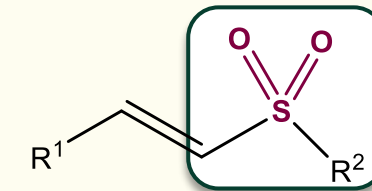
Uvođenje sulfonske skupine na (hetero)aromatske spojeve



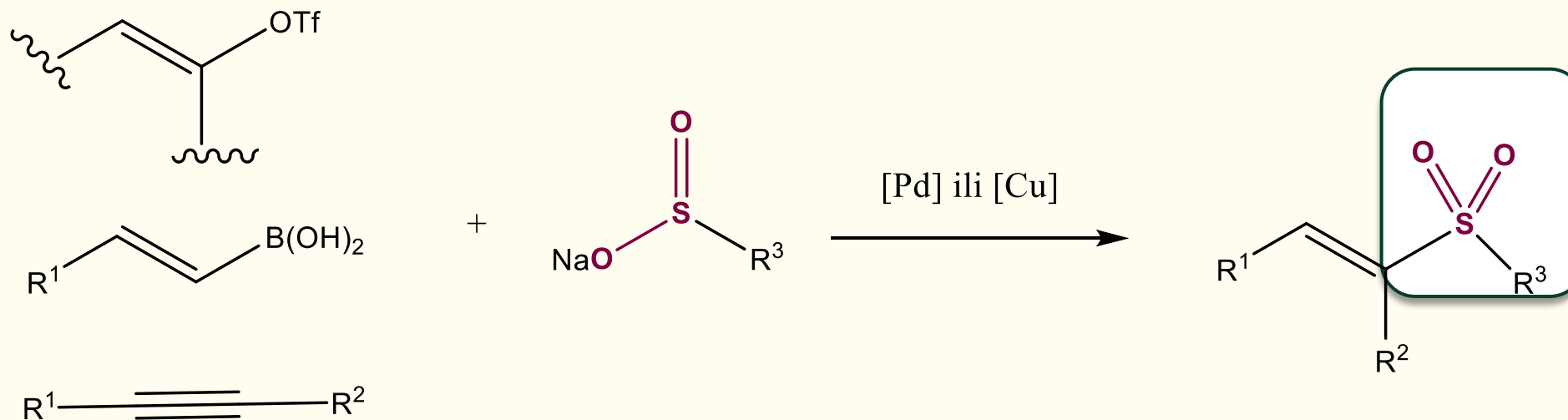
Slika 13. Mehanizam pripreme sulfonske skupine uz pomoć joda i sulfinatne soli



Sinteza nezasićenih sulfona



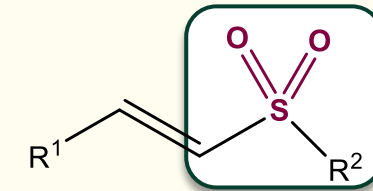
- ✓ Važni međuproducti u medicinskoj kemiji
- ✓ Moguća sinteza Michaelovom adicijom – često teško dostupni reaktanti
- ✓ Potrebna alternativna metoda



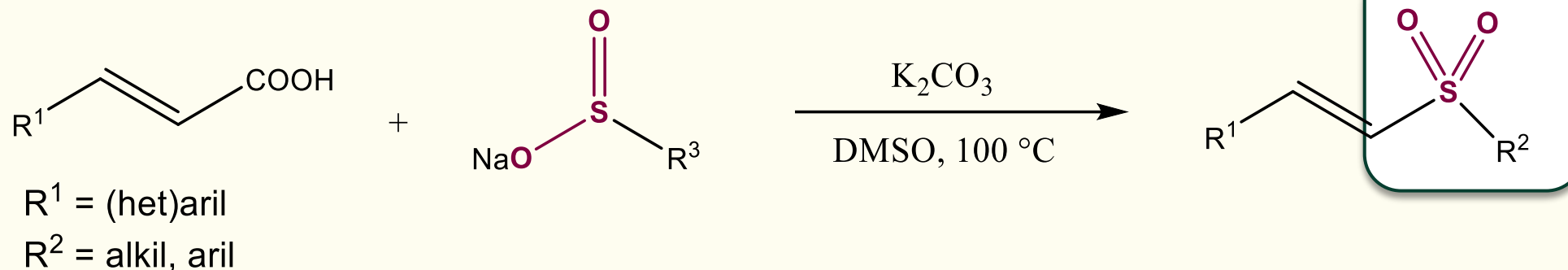
Slika 14. Načini priprave nezasićenih sulfona



Sinteza nezasićenih sulfona



Jiang:

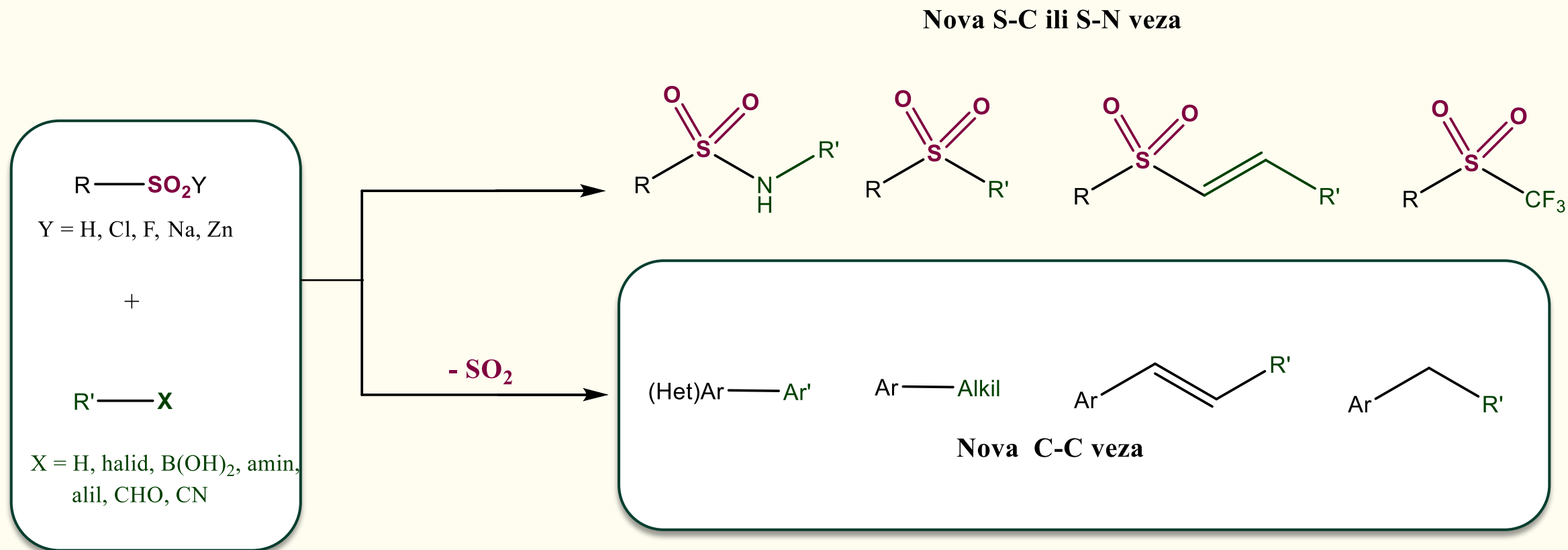


Slika 15. Način priprave nezasićenih sulfona

- ✓ Nije potrebna uporaba metala
- ✓ Lako dostupni reaktanti
- ✓ Visoka tolerancija funkcijskih skupina

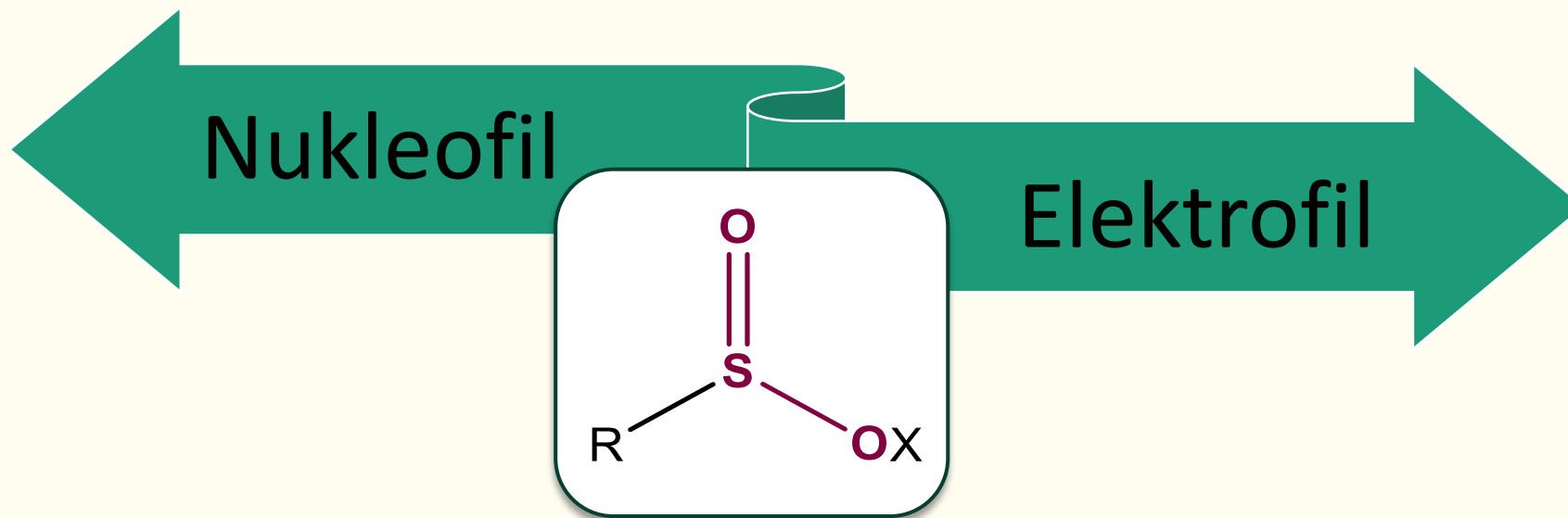
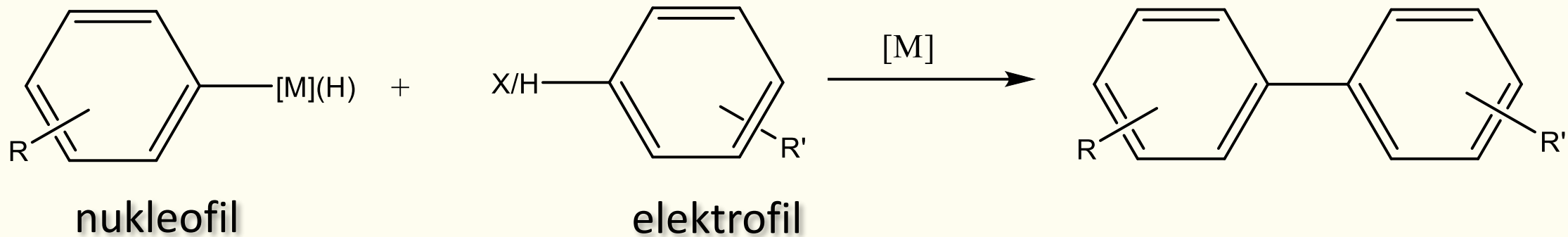


Reakcije sulfinata



Slika 16. Opći prikaz reakcija sulfinata

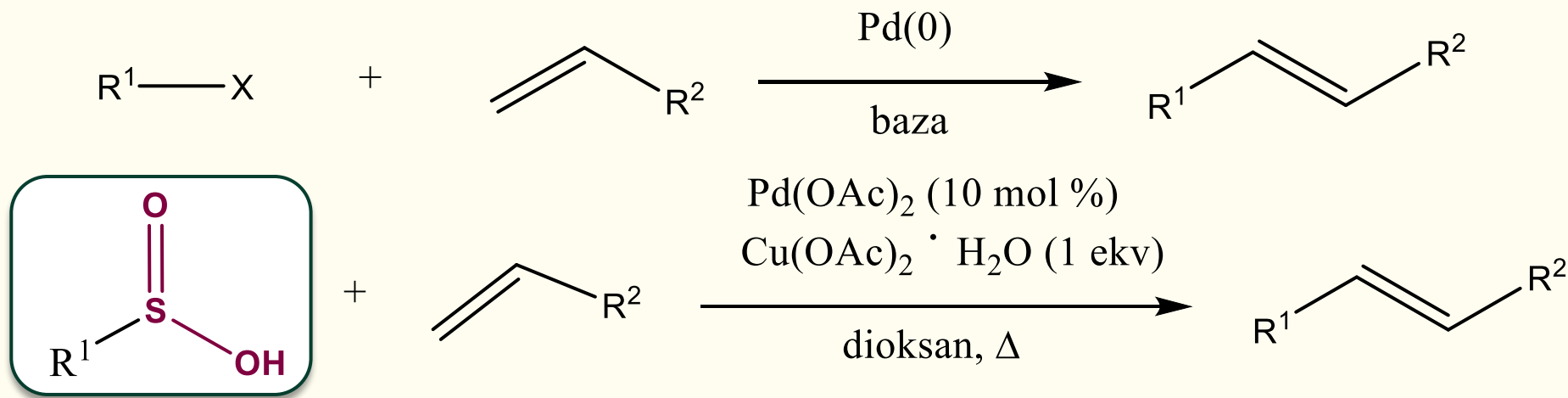
💡 Reakcije nastanka ugljik-ugljik veze



Slika 17. Opći prikaz reakcije unakrsnog povezivanja (gore) i sulfinatnog derivata (dolje)



Sulfinati u Heckovoj reakciji



R^1 = Aril, benzil

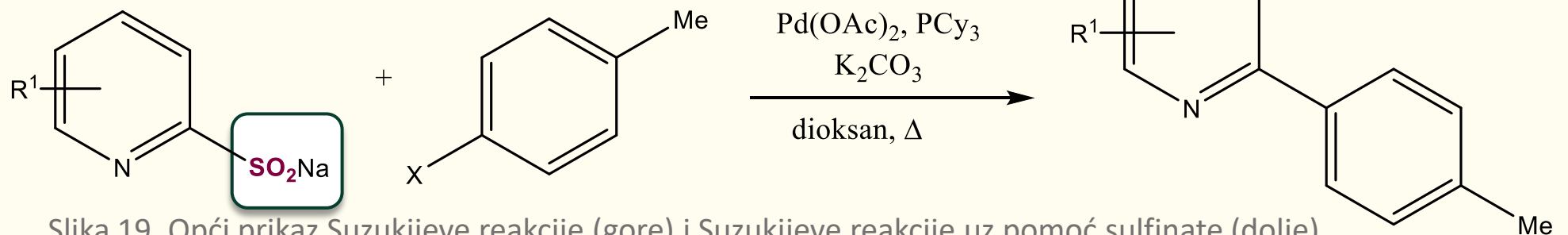
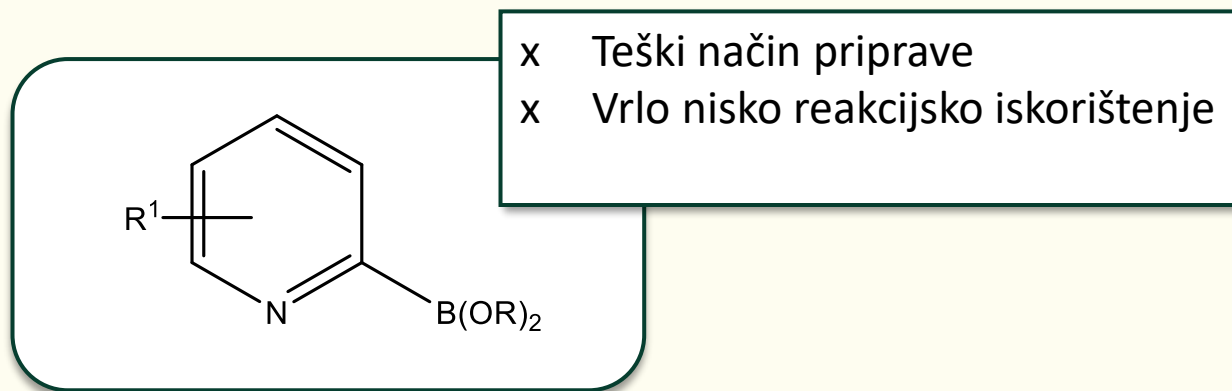
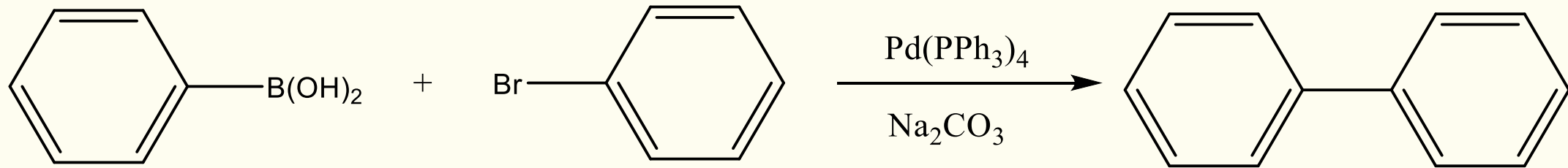
R^2 = Ph, *p*-MeC₆H₄, *p*-Cl-C₆H₄, CO₂Me, CO₂*n*Bu

X = Cl, Br, I, OTf, OTs

- ✓ Blaži reakcijski uvjeti
- ✓ Bez potrebe za uporabom baze

Slika 18. Heckova reakcija (gore) te Heckova reakcija provedena uz sulfinat kao polazni reagens (dolje)

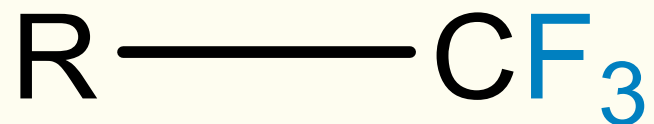
Sulfinati u Suzukijevoj reakciji



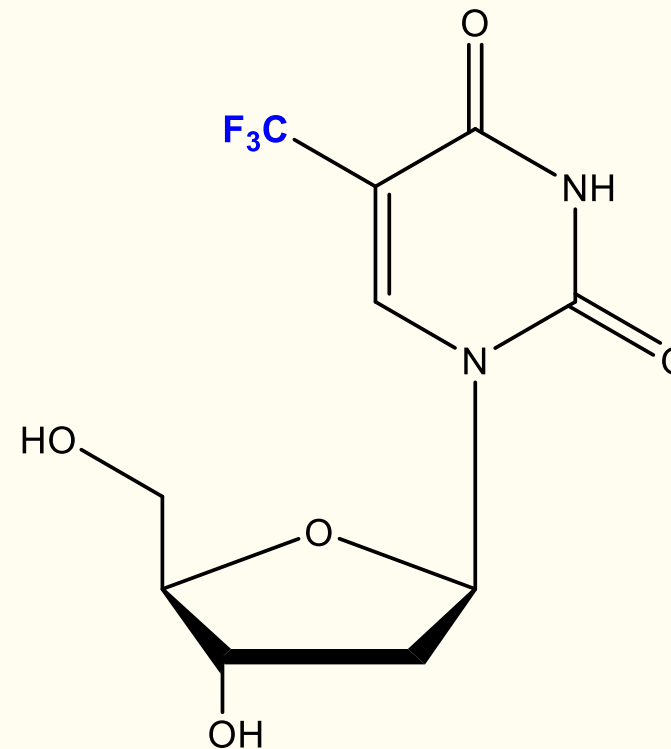
Slika 19. Opći prikaz Suzukijeve reakcije (gore) i Suzukijeve reakcije uz pomoć sulfinata (dolje)



Fluoriranje heterocikličkih spojeva



- ✓ Česti molekularni fragment u biološki važnim spojevima
- ✓ Za uvođenje obično potrebni korozivni fluorirajući reagensi

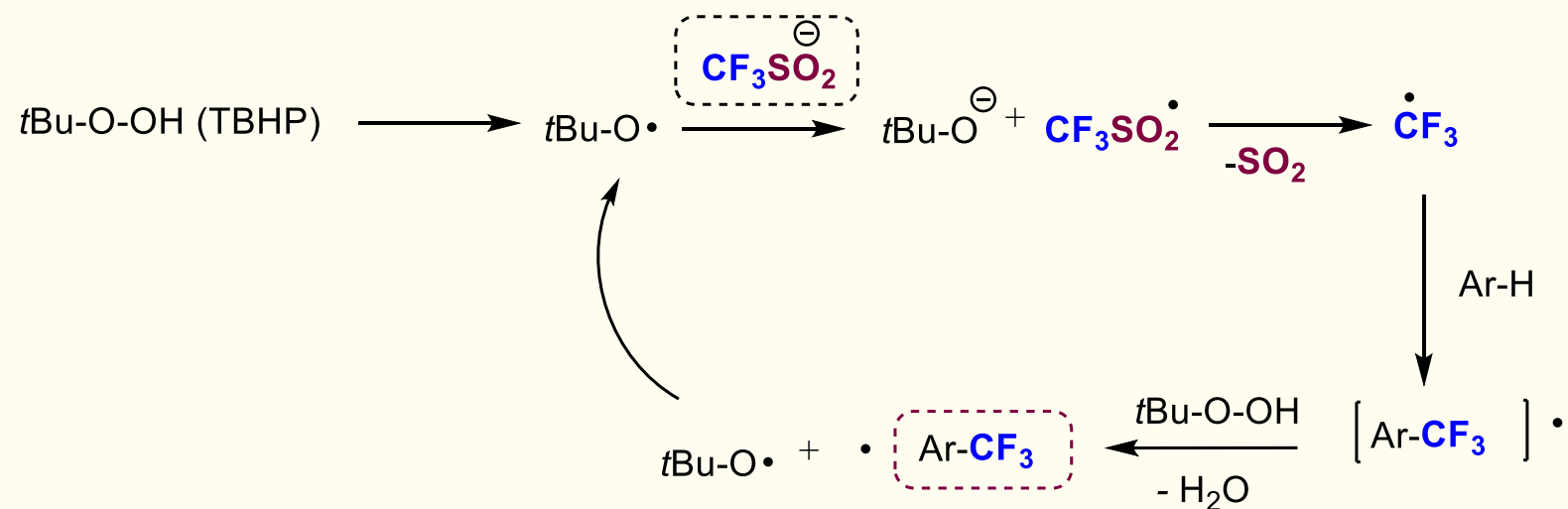
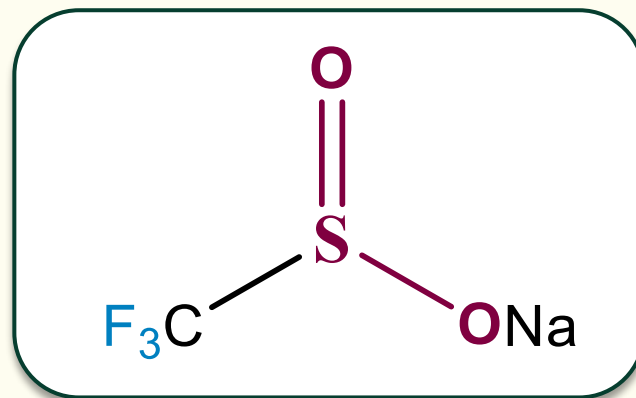


Slika 20. Struktura CF_3 skupine (lijevo) i trifluoridina (desno)



Fluoriranje heterocikličkih spojeva

Langloisov reagens:



Slika 21. Struktura Langloisovog reagensa (gore) i mehanizma uvođenja CF₃ fragmenta (dolje)

Zaključak:

- ✓ Sulfinati imaju ulogu u mnogim organskim reakcijama
- ✓ Još dosta neistraženo područje
- ✓ Poseban značaj prilikom sinteze sulfona/sulfonamida, ali i sinteze novih ugljik-ugljik veza
- ✓ Razvojem novih reagenasa raste i broj reakcija

Hvala na pažnji!!!