

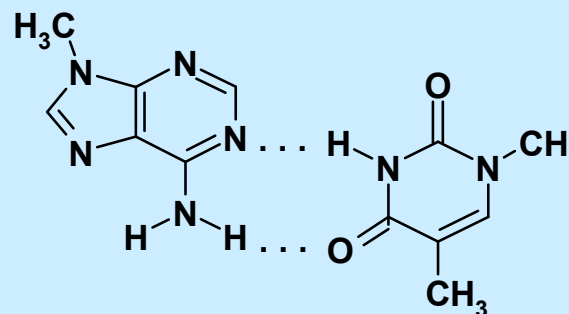
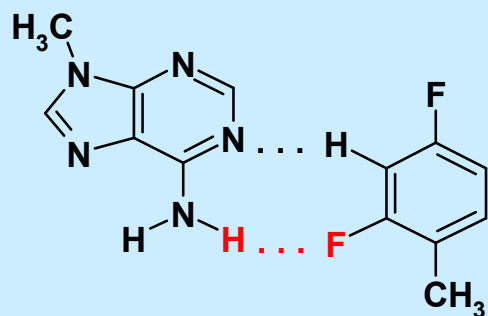


THE SYNTHESIS AND PROPERTIES OF FLUORINE-CONTAINING QUINOLONES, QUINAZOLINONES AND BENZOTHAZINONES

**Emiliya Nosova,
assistant professor (docent), doctorant
Urals State Technical University**

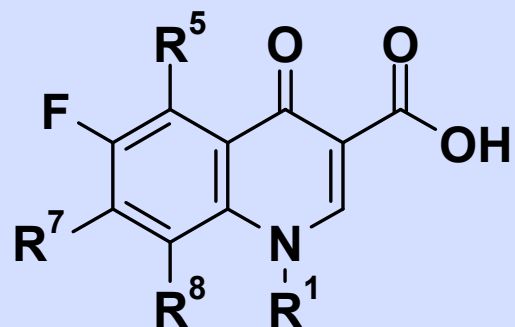
Fluorinated heterocycles as intriguing subjects for medicinal chemistry

Anticancer 5-fluorouracil, antimicotic fluconazol and antidepressant fluorobenzo-1,4-diazepine derivatives are just a few examples from the well-known series of fluorinated drugs.



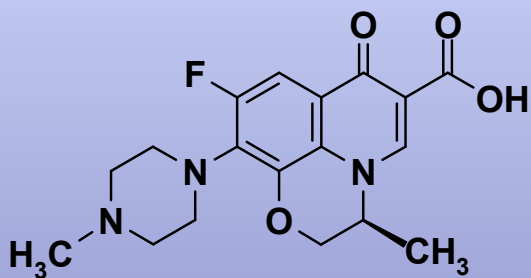
Some similarities between fluorinated arenes and DNA heterocyclic bases in electron density distribution and the ability for F...H hydrogen bond formation make fluorinated benzazoles and benzazines as intriguing subjects for medicinal chemistry.

BICYCLIC FLUOROQUINOLONES

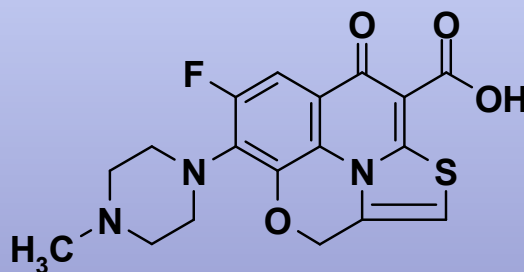


Ciprofloxacin,
Norfloxacin,
Pefloxacin,
Moxifloxacin,
Gatifloxacin,
Grepafloxacin

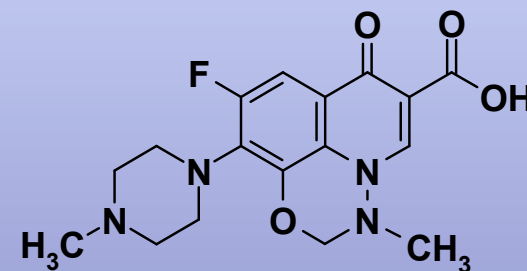
POLYCYCLIC FLUOROQUINOLONES



levofloxacin

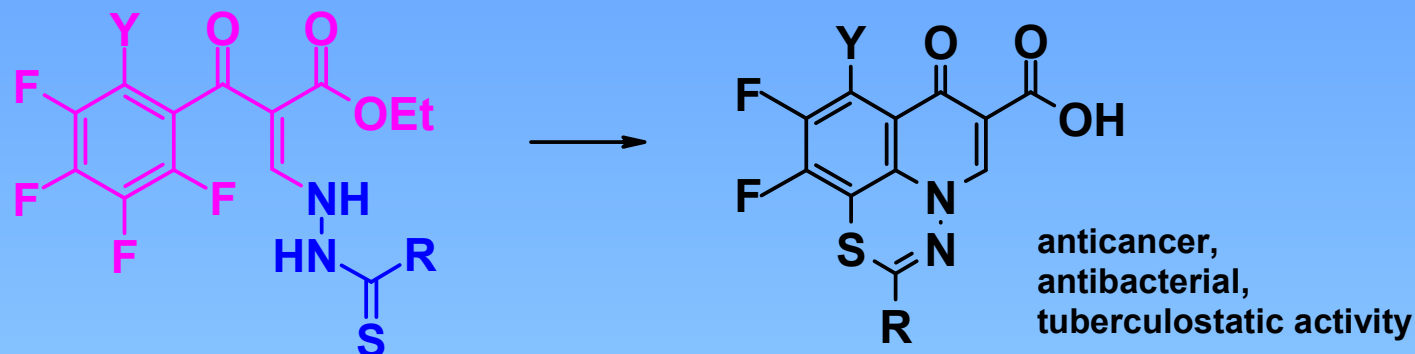


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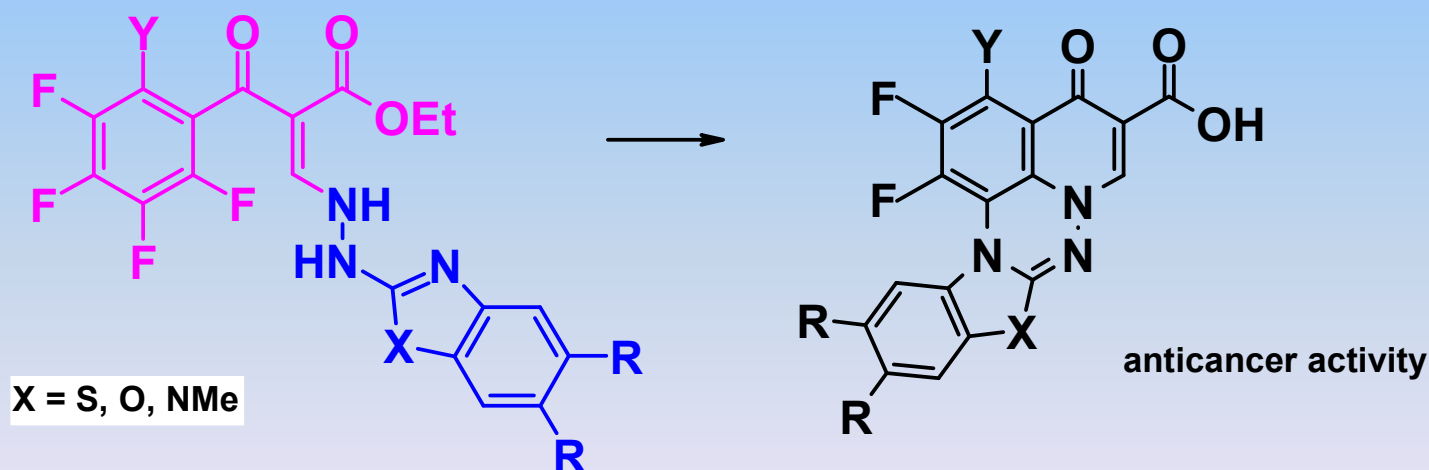


marbofloxacin

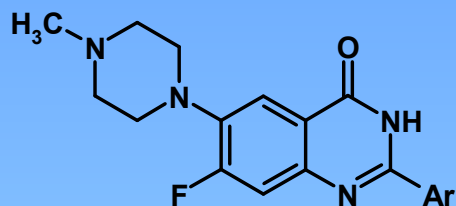
1,3,4-Thiadiazino[6,5,4-*i,j*]annelated fluoroquinolones



Pentacyclic fluoroquinolones

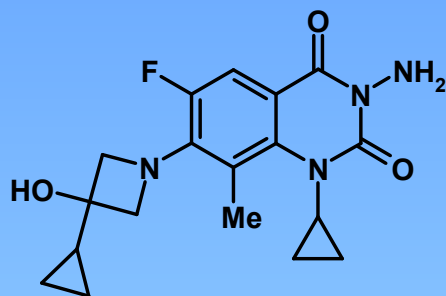


QUINAZOLINES POSSESING THE BIOLOGICAL ACTIVITY

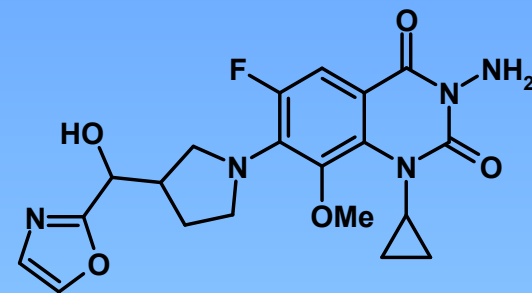


Heterocycles, 2005, p. 2061

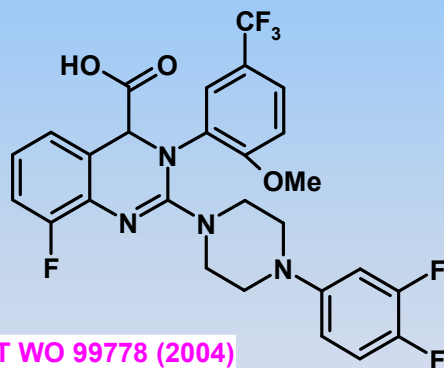
anticancer



PCT WO 26153, 26154 (2005)

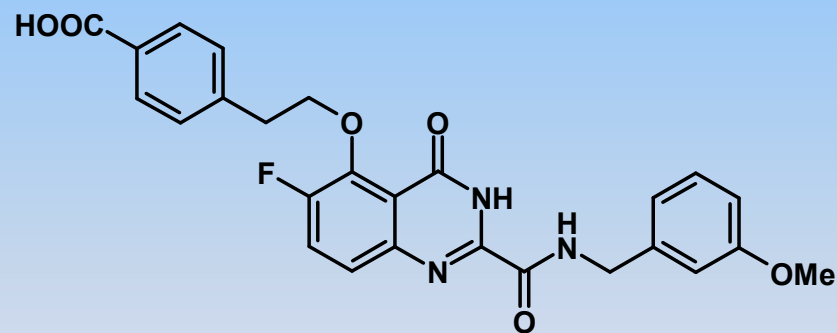


antibacterial



PCT WO 99778 (2004)

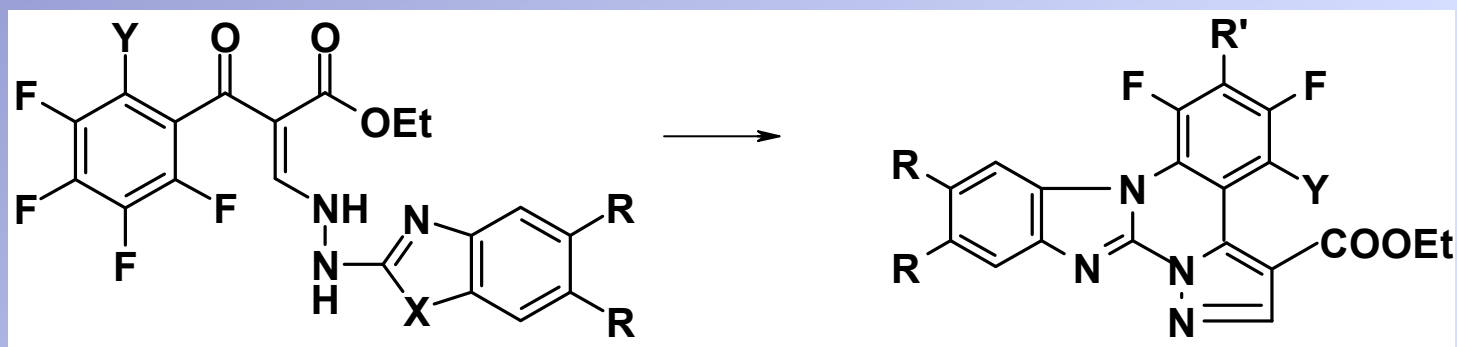
antiviral (cytomegalovirus)



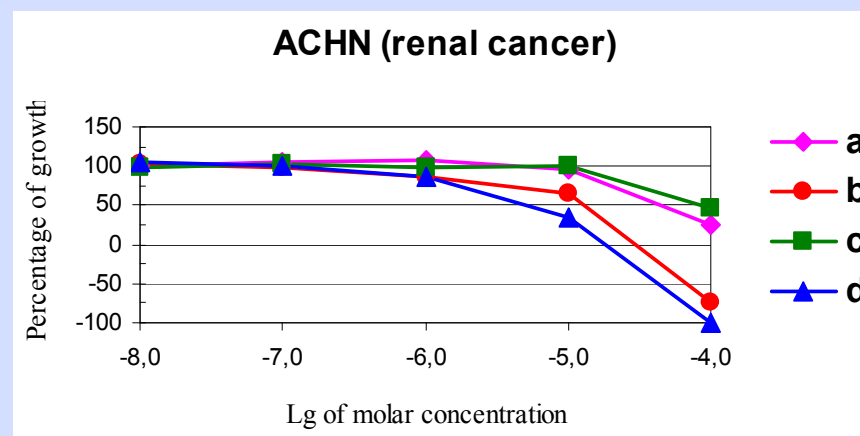
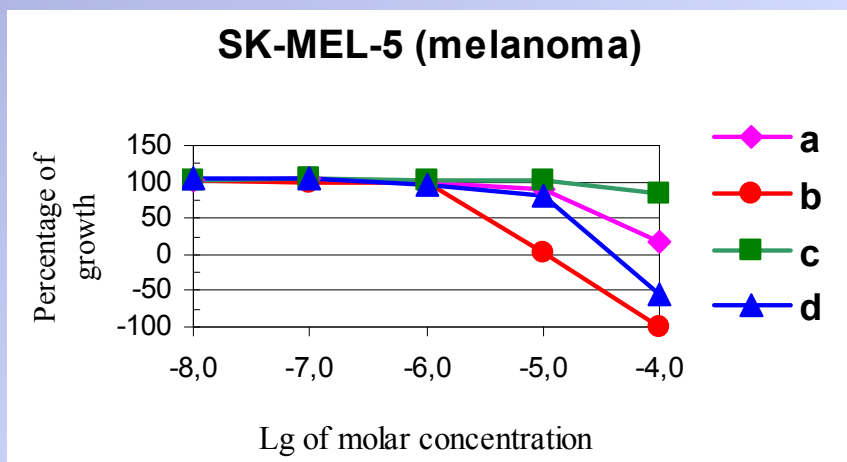
PCT WO 105760 (2005)

arthritis treatment

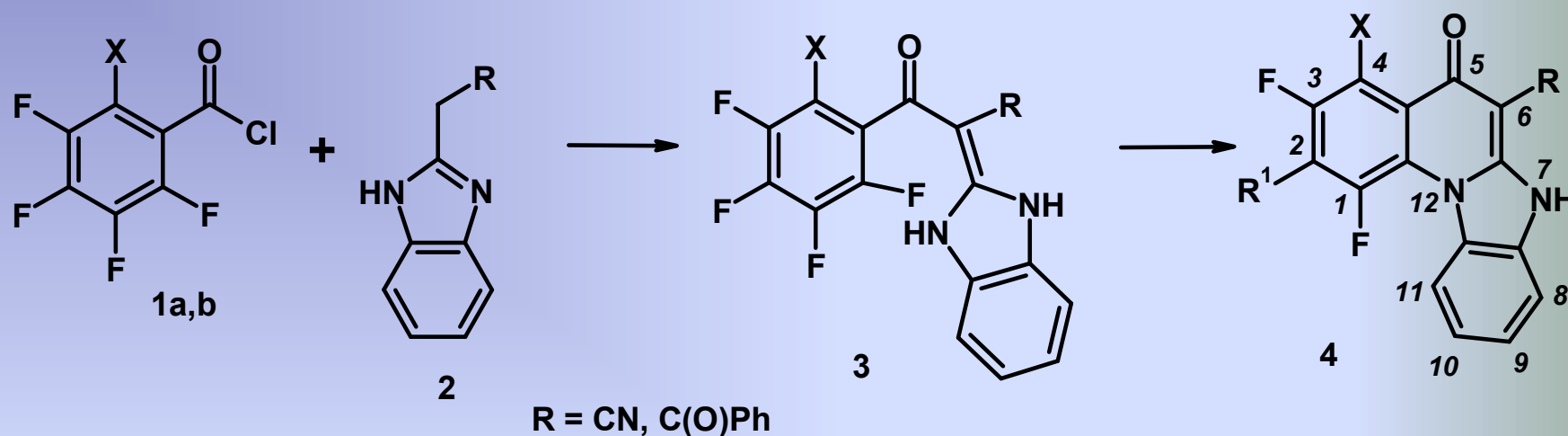
BENZIMIDAZO[1,2-*a*]PYRAZOLO[1,5-*c*]QUINAZOLINES



- a: Y = H, R = H, R' = F; b: Y = F, R = F, R' = F;
 c: Y = H, R = Br, R' = F; d: Y = H, R = H, R' = 4-methylpiperazin-1-yl

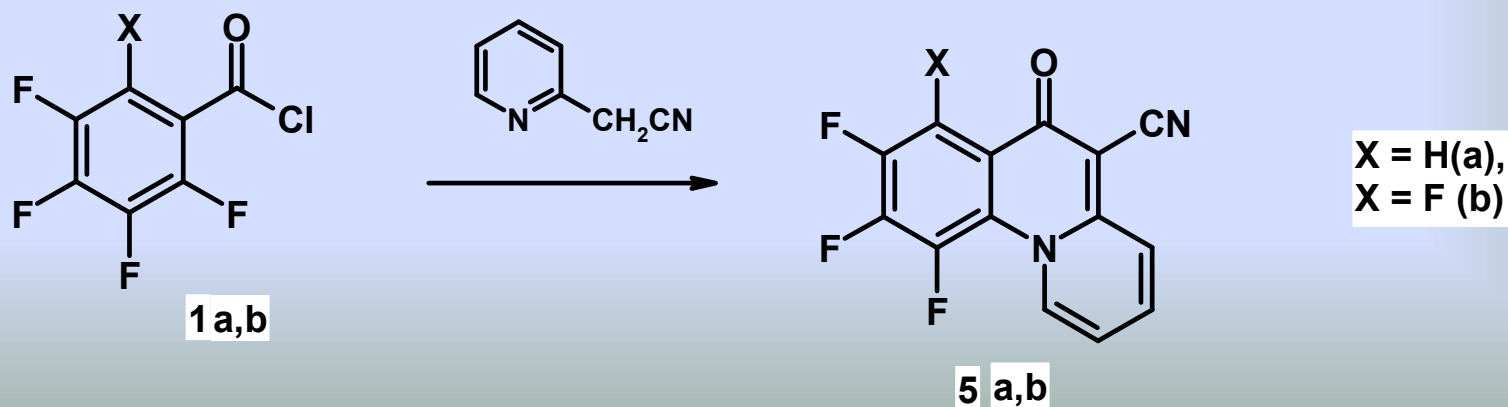


BENZIMIDAZO[1,2-*a*]FLUOROQUINOLONES

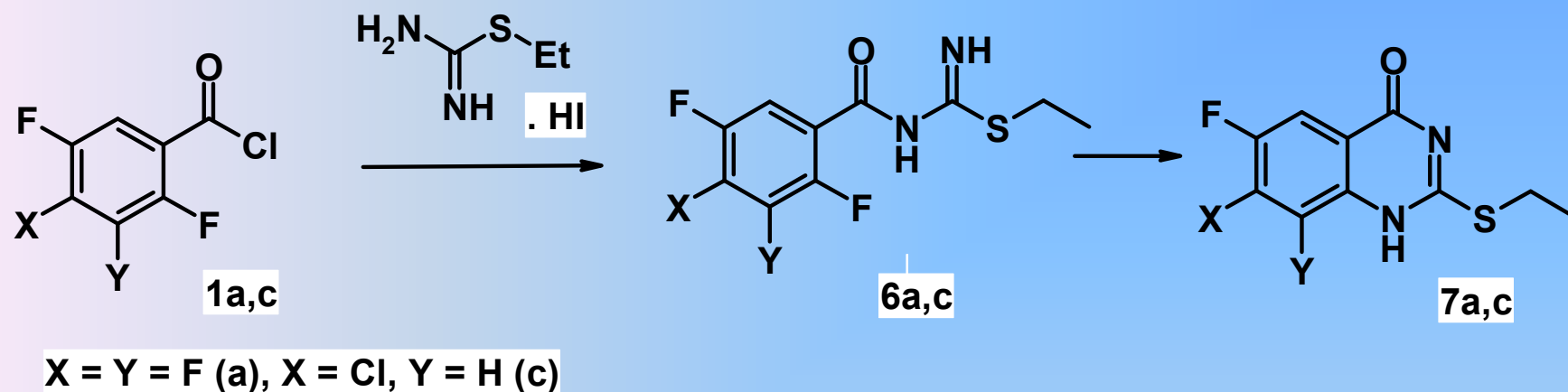


Derivative 4 (X = H, R = pyrrolidin-1-yl) exhibited the tuberculostatic activity (MIC 1.56 mkg/ml against *M. tuberculosis* H₃₇R_V)

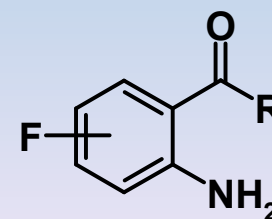
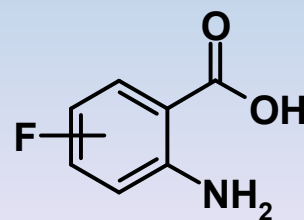
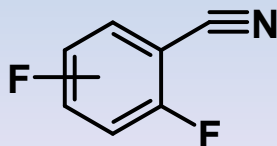
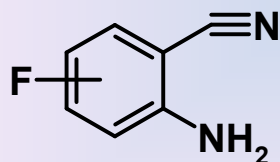
PYRIDO[1,2-*a*]FLUOROQUINOLONES



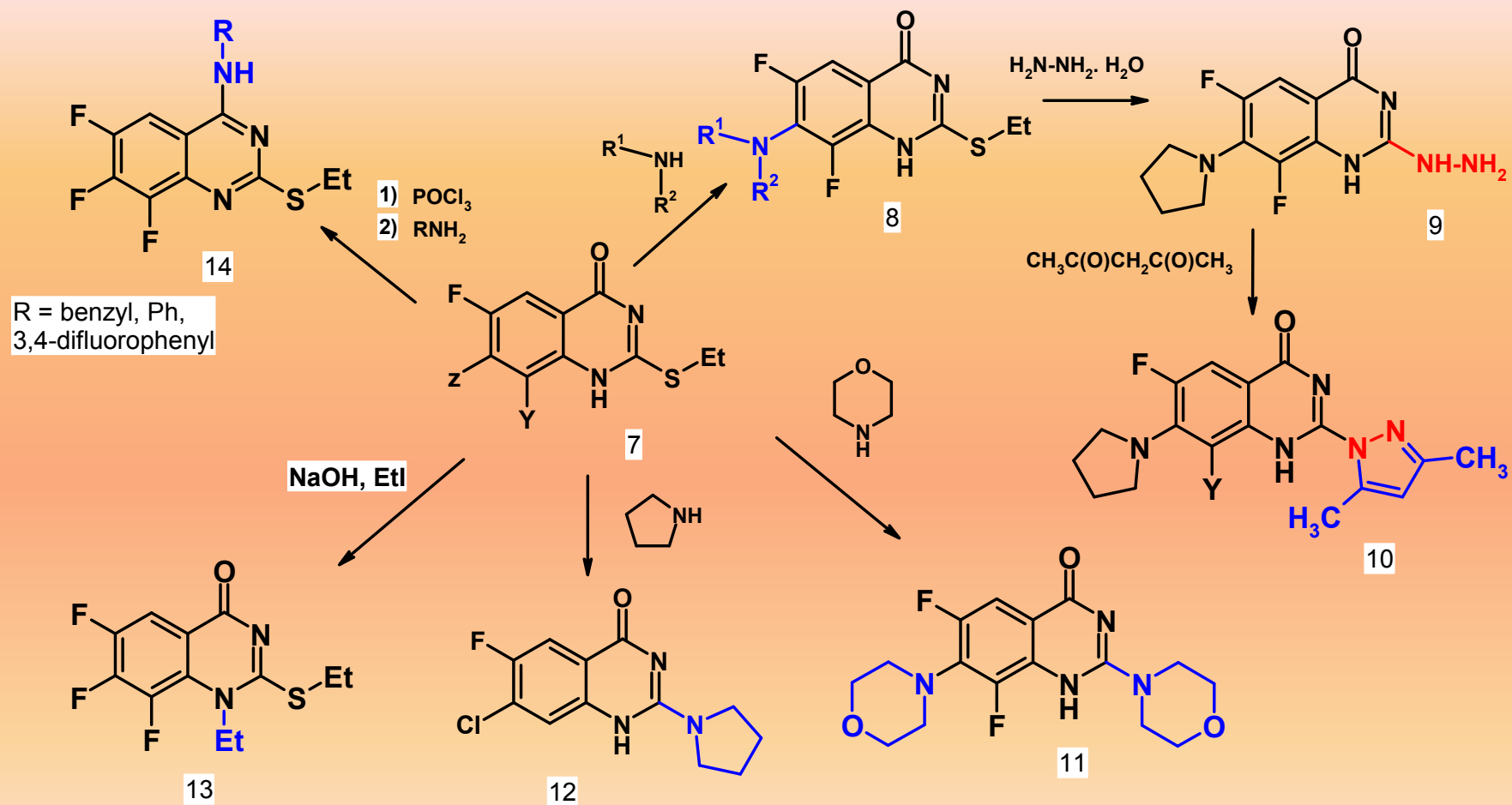
FLUORINATED 1H-QUINAZOLIN-4-ONES



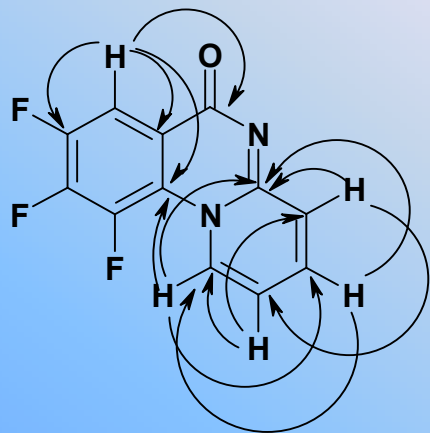
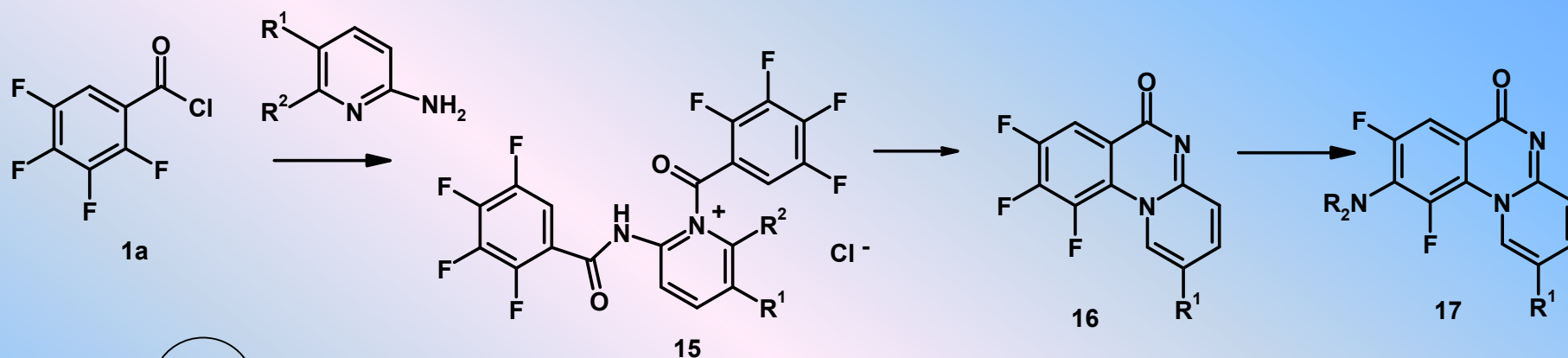
INTERMEDIATES FOR THE QUINAZOLINE SYNTHESIS KNOWN FROM THE LITERATURE



MODIFICATIONS OF 1H-QUINAZOLIN-4-ONES



FLUORINATED PYRIDO[1,2-*a*]QUINAZOLINONES



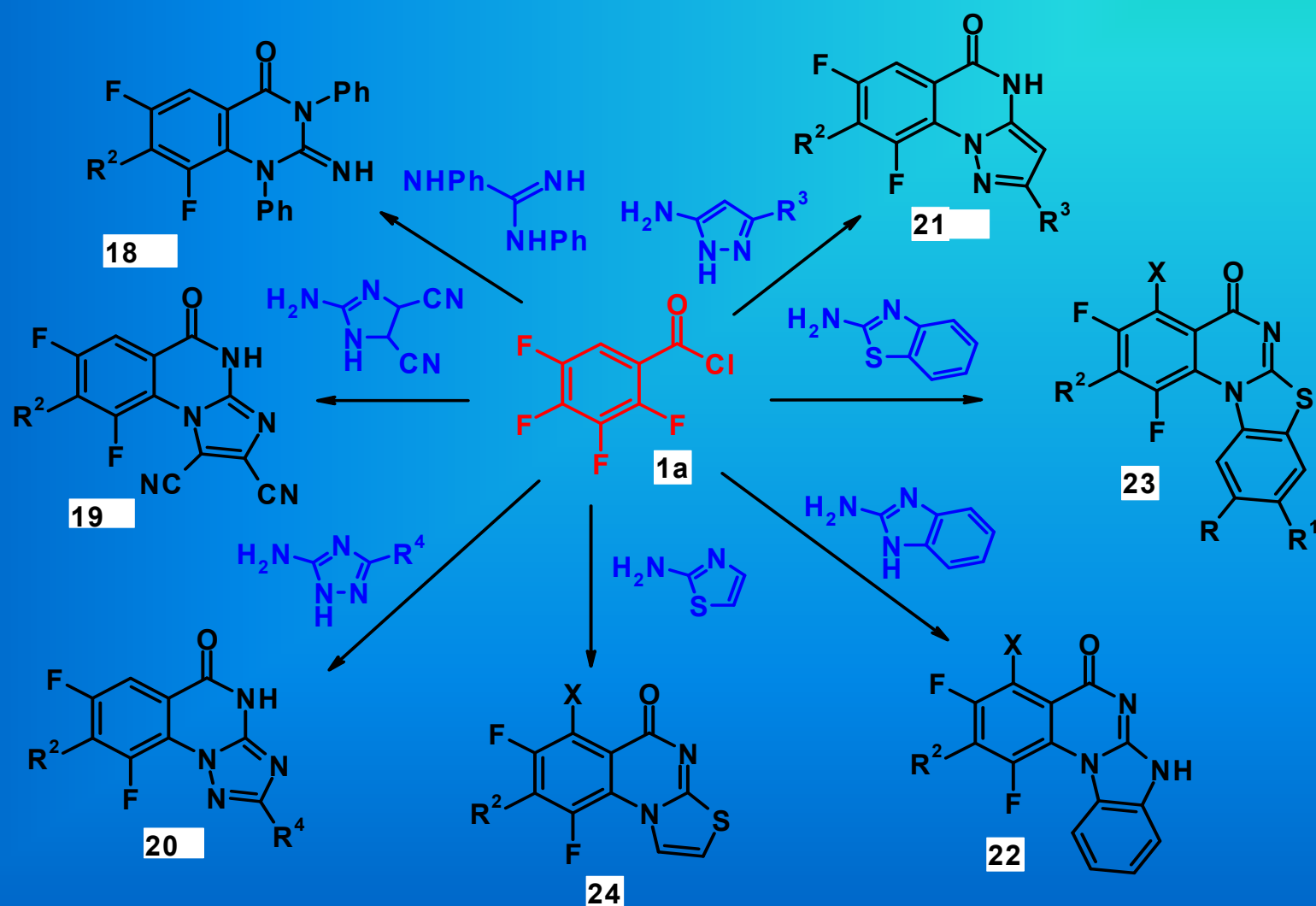
Data of heteronuclear
experiments HMBC

Tuberculostatic activity

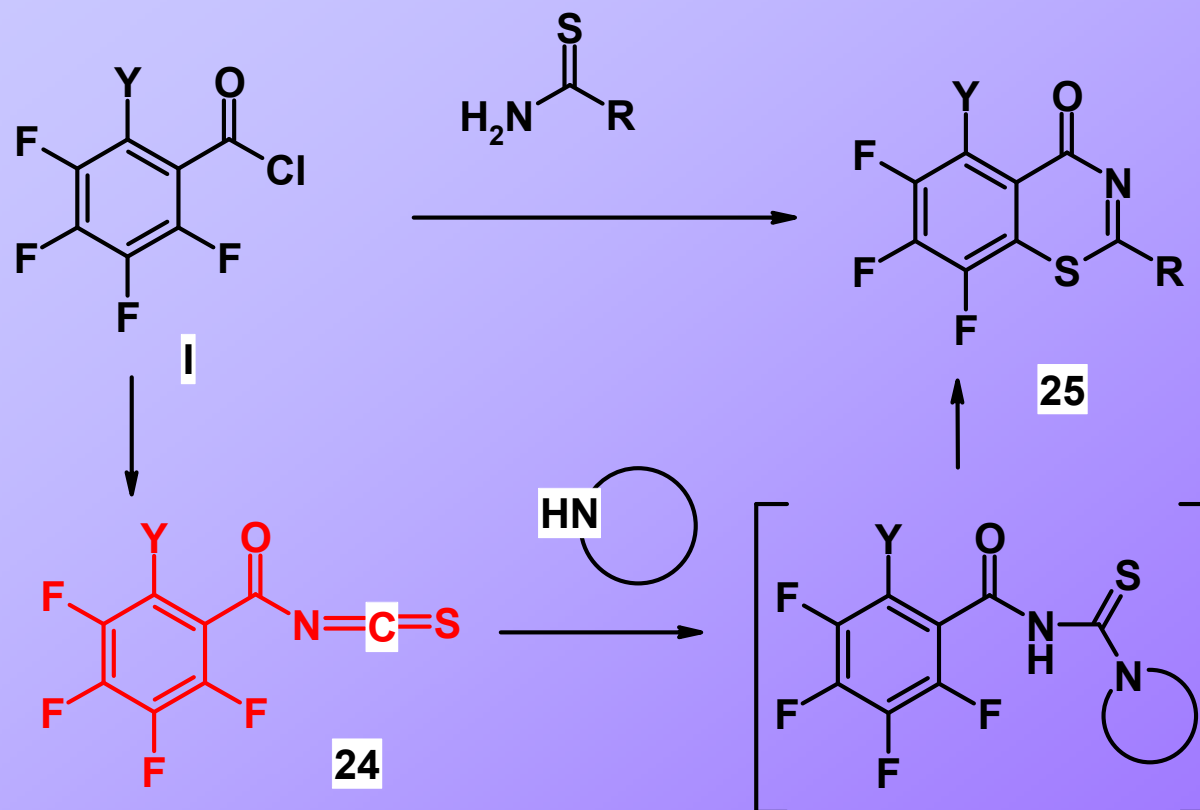
17 (NR₂ = morpholin-4-yl, R' = Me) MIC 1.56 mkg/ml

17 (NR₂ = 4-ethoxycarbonylpyperazin-1-yl, R' = Me) MIC 0.3 mkg/ml

FLUORINATED AZOLO- AND BENZAZOLO[1,2-*a*]QUINAZOLINONES



2-SUBSTITUTED [1,3]BENZOTHAZIN-4-ONES



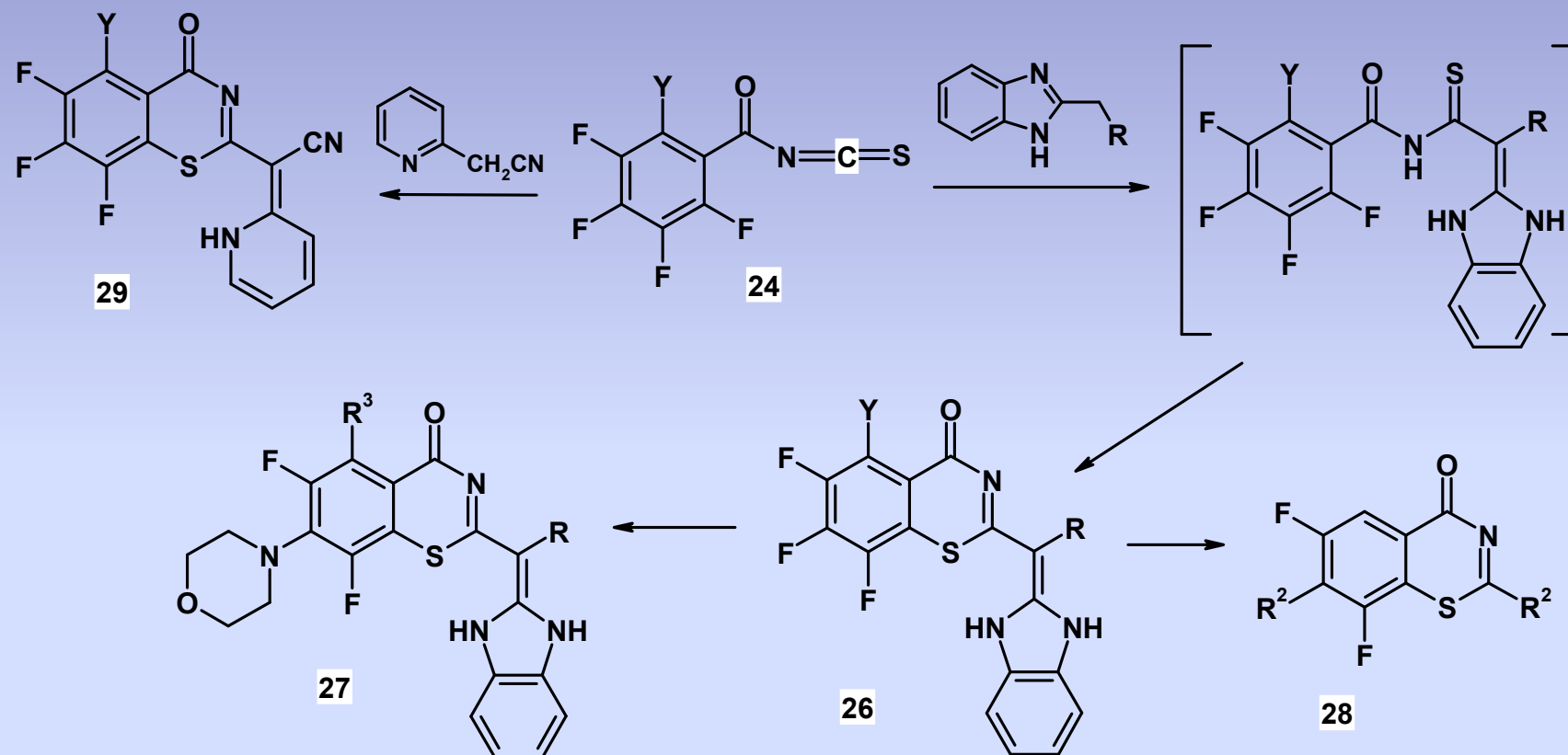
novel fluorinated building-block

Tuberculostatic activity

25 (R = 2-pyridyl, Y = H) MIC 0.3 mkg/ml

R = Ar, 2-pyridyl,
cycloalkylimino

(Polyfluorobenzoyl)isothiocyanates in reactions with CH-reactive benzoimidazoles and pyridines

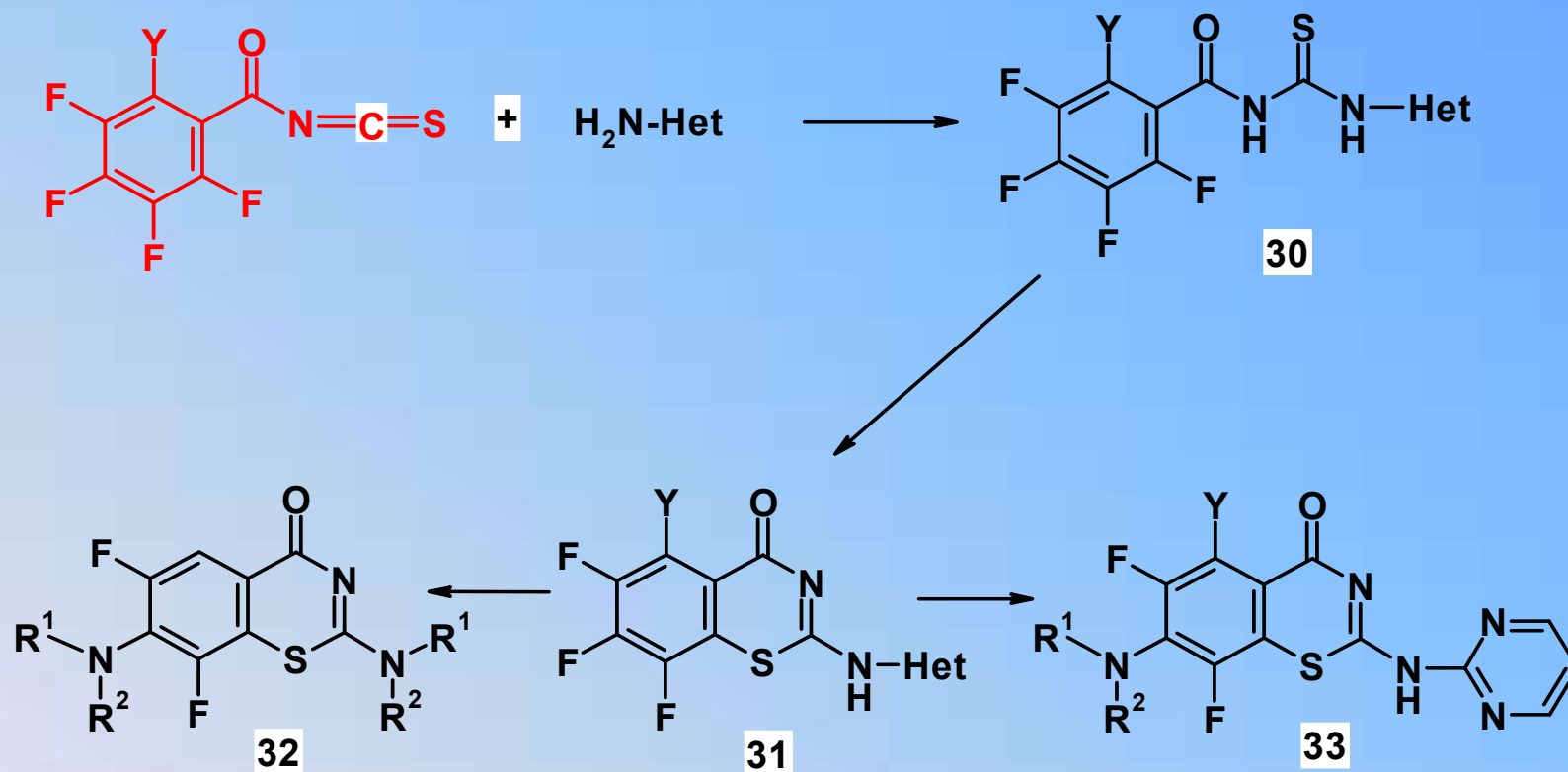


Tuberculostatic activity

28 (R2 = morpholin-4-yl) MIC 0.3 mkg/ml;

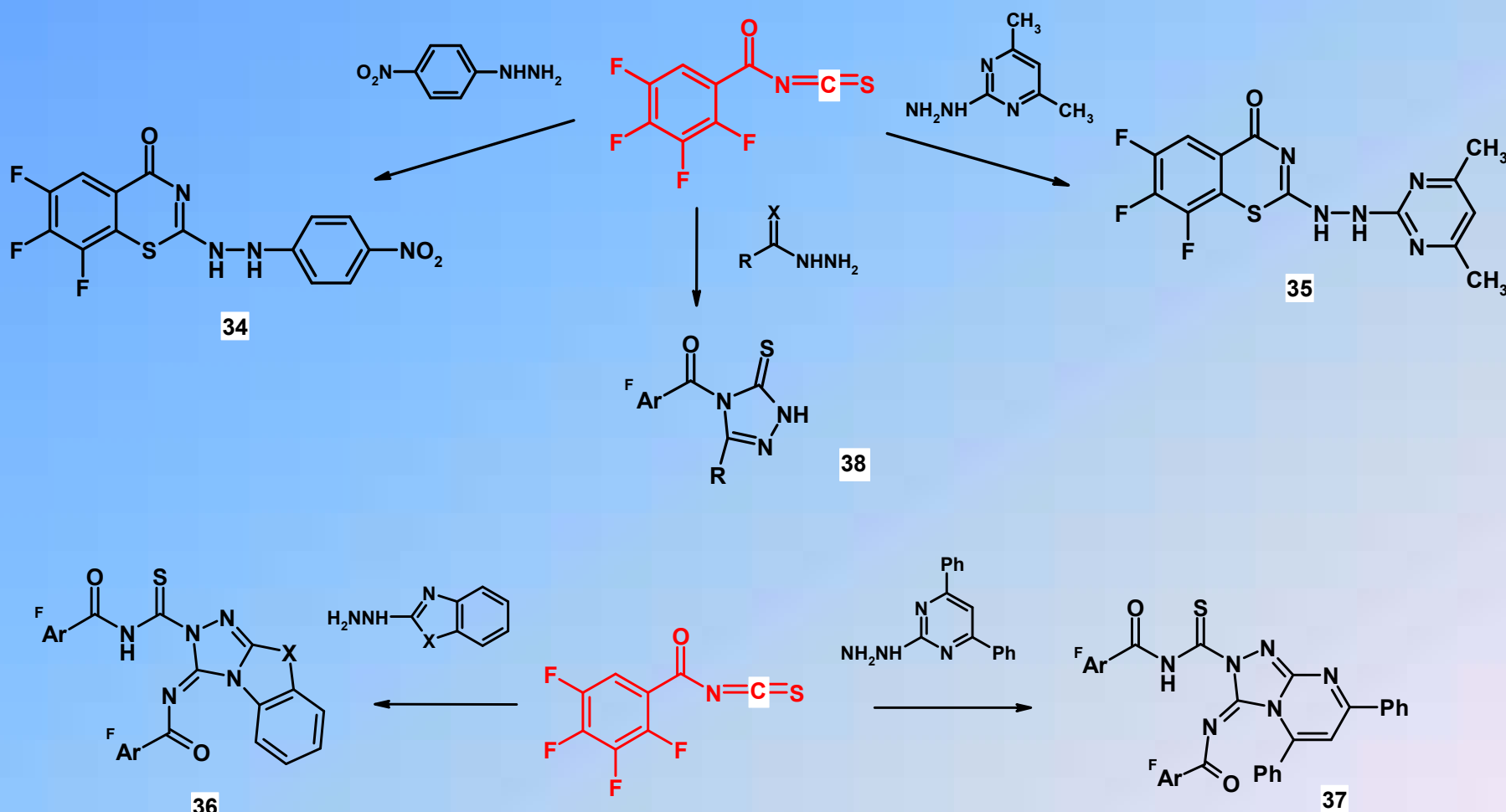
26 (R = CN, Y = H) MIC 0.3 mkg/ml

POLYFLUOROBENZOYLISOTHIOCYANATES IN REACTIONS WITH AMINOAZINES AND AMINOAZOLES



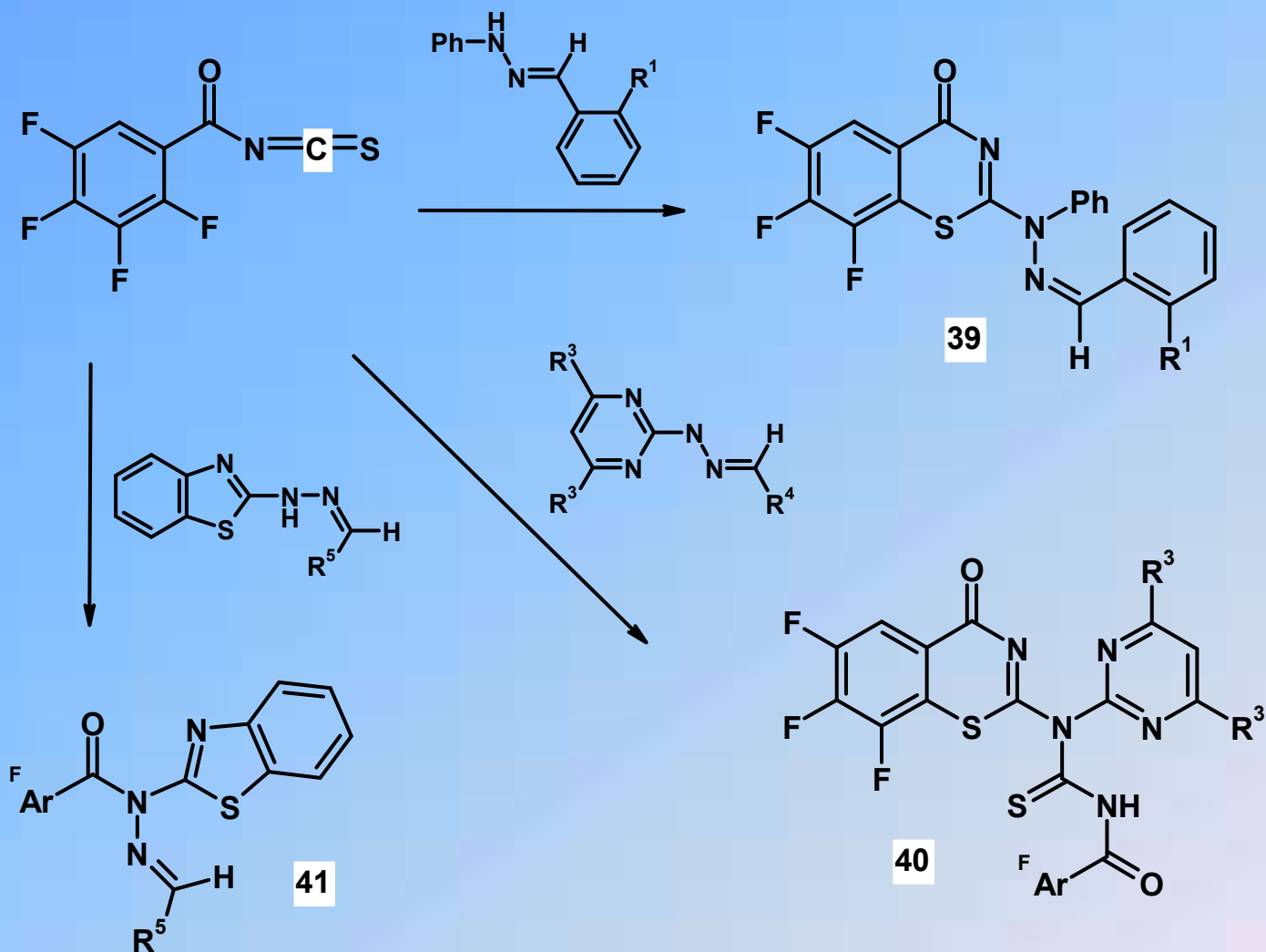
Het = pyridin-2-yl, pyrimidin-2-yl, 5-phenylpyrazol-3-yl

POLYFLUOROBENZOYLISOTHIOCYANATES IN REACTIONS WITH HYDRAZINES AND HYDRAZIDES

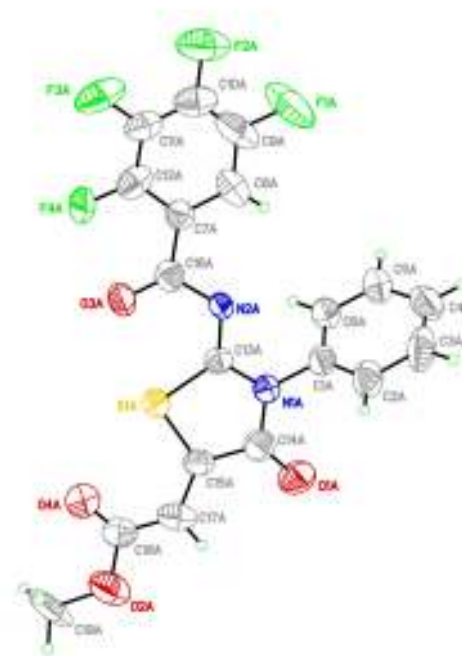
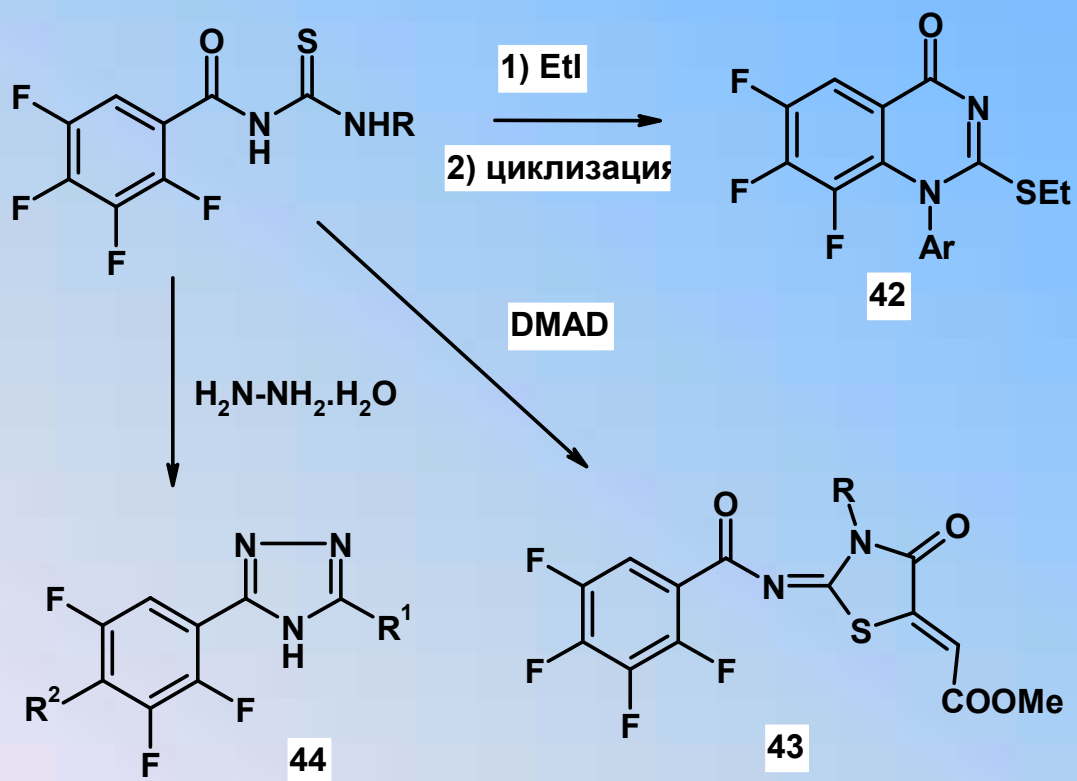


Tuberculostatic activity **36** (X = S) MIC 0.62 mkg/ml

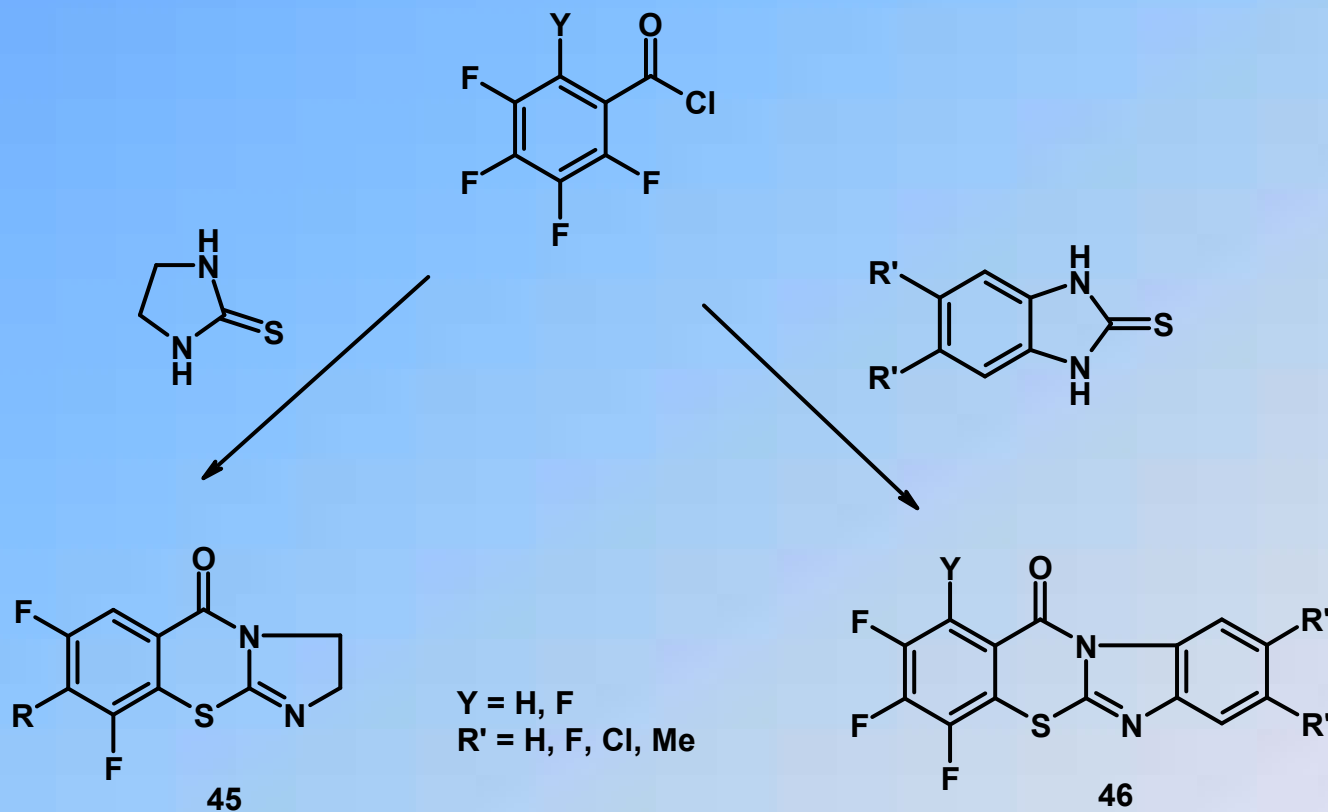
POLYFLUOROBENZOYLISOTHIOCYANATES IN REACTIONS WITH HYDRAZONES



(TETRAFLUOROBENZOYL)THIOUREAS IN THE SYNTHESIS OF FLUORINATED AZAHETEROCYCLES



IMIDAZO[2,1-*b*]BENZOTHAZINONES



Tuberculostatic activity 45 (R = morpholin-4-yl) MIC 0.1 mkg/ml